PATENT
Attorney Docket No. 8707-2165
168 – Apnée et PEA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Marcel LIMOUSIN and Guido GAGGINI
Title:	IMPROVED MANAGEMENT OF RESPIRATORY PAUSES OR HYPOPNEA IN AN ACTIVE IMPLANTABLE MEDICAL DEVICE OF THE CARDIAC PACEMAKER, DEFIBRILLATOR, CARDIOVERTOR OR MULTISITE DEVICE TYPE
Serial No.:	10/693,833
Filed:	October 24, 2003
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Examiner:	Stephanie R. Smith
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Date of Action:	August 15, 2007

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P.O. Box 1450
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APPEAL BRIEF

This is an appeal to the Board of Patent Appeals and Interferences from a Final Action dated August 15, 2007. A Notice of Appeal was timely filed on February 14, 2008.

The undersigned authorizes a charge to Deposit Account No. 15-0665 in the amount of $510.00 for the filing of this Appeal Brief (pursuant to 37 C.F.R. § 41.20(b)(2)) in the above-identified application. The undersigned also authorizes any additional fees which may be required, or credit any overpayment, to Deposit Account No. 15-0665.

Applicants submit this Appeal Brief in accordance with 37 C.F.R. § 41.37.

I. REAL PARTY IN INTEREST

The real party in interest is ELA MEDICAL S.A.S., a corporation organized and existing under and by virtue of the laws of France, and having its principal place of business at 98 Rue Maurice-Arnoux, F-92120, Montrouge France, the assignee of record, which is a subsidiary of Sorin S.p.A. Via Benigno Crespi, 17, 20159 Milano, Italy.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF CLAIMS

Claims 1–13 are pending in the application. Claims 1–13 stand rejected and each is appealed.

IV. STATUS OF AMENDMENTS

Applicants filed a response after final action on February 13, 2008. In the response, Applicants traversed the rejection of claims 1–13 under 35 U.S.C. § 112, first paragraph; traversed the rejection of claims 1–5 and 11–13 under U.S.C. § 102(b); and traversed the rejection of claims 6–10 under U.S.C. § 103(a). The Examiner did not file a written reply to Applicants' response after final action, but after a telephone conference on July 22, 2008, the Examiner indicated by voicemail on July 24, 2008 her intention to maintain the rejection of claims 1–13 under § 112, first paragraph. Further attempts to reach the Examiner regarding the other grounds for her rejections were not responded to.

V. SUMMARY OF CLAIMED SUBJECT MATTER

There is one independent claim to a defined apparatus (claim 1), 9 dependent claims to the apparatus of claim 1 (claims 2–6, 8–10, and 13); 2 dependent claims to the apparatus of claim 2 (claims 11–12); and 1 dependent claim to the apparatus of claim 6 (claim 7).

Claim 1 is directed to an active implantable medical device for measuring and processing ventilatory activity and hemodynamic activity, and then treating any detected apnea or hypopnea. (page 1, lines 2–6; page 3, 12–16) Such a device includes (1) means for measuring respiratory activity having an output signal representative of ventilatory activity of the patient (page 4, lines 9–14; page 7, lines 3–12); (2) means for analyzing the ventilatory activity signal and detecting an occurrence of a respiratory apnea and an occurrence of a respiratory hypopnea (page 4, lines 9–14; page 8, lines 1–7); (3) means for measuring a hemodynamic state having an output hemodynamic signal representative of the contractility of the myocardium (page 4, lines 15–20; page 8, line 13 to page 9, line 3); (4) means for analyzing the hemodynamic signal and detecting an occurrence of a variation of the contractility (page 4, lines 15–20; page 8, lines 8–12; page 5, lines 4–5); (5) means for determining whether the detected contractility variation is significant (page 4, lines 15–20; page 11, lines 4–9); and (6) means for conditionally modifying an operating parameter of the device to treat a detected apnea or hypopnea when said detected contractility variation is significant (page 3, 17–22; page 4, lines 15–20; page 5, lines 6–9).

The corresponding structure for the (1) "means for measuring respiratory activity" and the (2) "means for analyzing the ventilatory activity signal" consists of "an implantable medical device that includes circuit structure and functionality able to measure the respiratory activity and deliver a signal representative of ventilatory activity of the patient" and "circuit means for

analyzing the ventilatory activity signal," both of the type that described by European Patent No. EP 0 970 713 and U.S. Patent No. 6,574,507. (page 4, lines 9–14).

The corresponding structures for the (3) "means for measuring a hemodynamic state" are "an endocardial acceleration sensor of the type PEA" as described in European Patent No. EP 0 515 319 and U.S. Patent Nos. 5,304,208, 5,454,838, and 5,496,351 and for sale under the trade name Living CHF and Best by Sorin Biomedica Cardio SpA (page 8, line 13–20) and "a sensor of endocardiac impedance" such as "transvalvular bio-impedance", as described by European Patent No. EP 1 116 497 and U.S. Patent No. 6,604,002 or "trans-septum bio-impedance," as described by European Patent No. EP 1 138 346 and U.S. Patent Publication No. 2001/0034540 (page 8, line 20 to page 9, line 3).

The corresponding structure to the (4) "means for analyzing the hemodynamic signal"; (5) "means for determining whether the detected contractility variation is significant"; and (6) "means for conditionally modifying an operating parameter of the device to treat a detected apnea or hypopnea" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19), and circuits for delivering stimulation pulses and multisite stimulation pulses as described in United States Patent No. 6,253,206 (page 3, lines 14–22, page 5, line 21 to page 6, line 4).

Claim 2 is directed to the active implantable medical device of claim 1 wherein the (5) means for determining whether the contractility variation is significant further comprises means for operating said analyzing means to analyze said hemodynamic signal detected after

detection of said apnea or hypopnea (page 5, lines 7–8). The corresponding structure to said "means for operating said analyzing means" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of recciving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 2 is directed to the active implantable medical device of claim 1 wherein the (5) means for determining whether the contractility variation is significant further comprises means for operating said analyzing means to analyze said hemodynamic signal detected before detection of said apnea or hypopnea (page 5, lines 7–8). The corresponding structure to said "means for operating said analyzing means" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 4 is directed to the active implantable medical device of claim 1 wherein the (3) hemodynamic measuring means further comprises means for measuring an intracardiac impedance. (page 5, lines 4–5.) The corresponding structures to the (3) "hemodynamic measuring means" are "an endocardial acceleration sensor of the type PEA" as described in European Patent No. EP 0 515 319 and U.S. Patent Nos. 5,304,208, 5,454,838, and 5,496,351 and for sale under the trade name Living CHF and Best by Sorin Biomedica Cardio SpA (page 8, line 13–20), and "a sensor of endocardiac impedance" such as "transvalvular bio-impedance", as described by Eupropean Patent No. EP 1 116 497 and U.S. Patent No. 6,604,002 or "trans-

septum bio-impedence," as described by European Patent No. EP 1 138 346 and U.S. Patent Publication No. 2001/0034540 (page 8, line 20 to page 9, line 3).

Claim 5 is directed to the active implantable medical device of claim 1 wherein the (3) hemodynamic measuring means further comprises means for measuring an endocardial acceleration. (page 5, lines 4–5.) The corresponding structures to the (3) "hemodynamic measuring means" are "an endocardial acceleration sensor of the type PEA" as described in European Patent No. EP 0 515 319 and U.S. Patent Nos. 5,304,208, 5,454,838, and 5,496,351 and for sale under the trade name Living CHF and Best by Sorin Biomedica Cardio SpA (page 8, line 13–20), and "a sensor of endocardiac impedance" such as "transvalvular bio-impedance," as described by European Patent No. EP 1 116 497 and U.S. Patent No. 6,604,002 or "trans-septum bio-impedance," as described by European Patent No. EP 1 138 346 and U.S. Patent Publication No. 2001/0034540 (page 8 line 20 to page 9 line 3).

Claim 6 is directed to the active implantable medical device of claim 1 wherein said operating parameter has a first value and said conditionally modifying means further comprises means for modifying in a temporary manner said operating parameter to a second value different from said first value. (page 10, lines 15–20.) The corresponding structure to "means for modifying in a temporary manner said operating parameter" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 7 is directed to the active implantable medical device of claim 6 wherein said (6) conditionally modifying means further comprises means for restoring said operating

parameter to said first value in response to said hemodynamic signal analysis means no longer detecting a variation of myocardium contractility. (page 10, lines 10–14). The corresponding structure to "means for restoring said operating parameter to said first value" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 8 is directed to the active implantable medical device of claim 1 wherein said operating parameter is a stimulation frequency, and said conditional modification is an increase in response to a detected significant variation and a detected apnea or hypopnea. (page 5, lines 11–13.)

Claim 9 is directed to the active implantable medical device of claim 1 wherein said operating parameter is an atrio-ventricular delay and said conditional modification is a shortened delay in relation to a detected significant variation and a detected apnea or hypopnea. (page 5, lines 14–16.)

Claim 10 is directed to the active implantable medical device of claim 1 wherein said device further comprises means for stimulating a patient's heart having at least a first stimulation mode for delivering a multisite stimulation, wherein said operating parameter is a mode of cardiac stimulation, and said conditional modification comprises means for operating said stimulation means to trigger a multisite stimulation in relation to said detected significant variation and a detected apnea or hypopnea. (page 5, line 17 to page 6, line 4.) The corresponding structure to "means for stimulating a patient's heart" and "means for operating

said stimulation means to trigger a multisite stimulation" consists of a "multisite stimulation mode" as described in U.S. Patent No. 6,253,106. (page 5, line 21 to page 6, line 4).

Claim 11 is directed to the active implantable medical device of claim 2 wherein the (4) hemodynamic signal analyzing means further comprises means for comparing a first hemodynamic signal measured during a cardiac cycle following the respiratory cycle during which the apnea or hypopnea was detected, with an average of the hemodynamic signals acquired prior to said respiratory cycle. (page 6, lines 5–8.) The corresponding structure to "means for comparing a first hemodynamic signal" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a"microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 12 is directed to the active implantable medical device of claim 2 wherein the hemodynamic signal analyzing means further comprises means for comparing a first hemodynamic signal measured after a plurality of cardiac cycles following the respiratory cycle during which the apnea or hypopnea was detected with an average of the hemodynamic signals acquired prior to said respiratory cycle during which the apnea or hypopnea was detected. (page 6, lines 9–13.) The corresponding structure to "means for comparing a first hemodynamic signal" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

Claim 13 is directed to the active implantable medical device of claim 1 wherein said device further comprises means for comparing a detected contractility variation to a reference threshold, and determining a significant variation in response to said contractility variation being greater than said threshold. (page 9, lines 12–18.) The structure for "means for comparing a detected contractility variation" consists of an "active implantable medical device[] available from Ela Médical, Montrouge France" that is a "microprocessor-based system[] having circuits for receiving, conditioning and processing detected electrical signals, . . . that [is] capable of receiving software instructions . . ., storing them in memory, and then executing those instructions to perform the [claimed] functions" (page 11, lines 14–19).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 1–13 are unpatentable under 35 U.S.C. § 112, first paragraph.

Whether claims 1–5 and 11–13 are unpatentable under 35 U.S.C. § 102(b) over Street et al., European Patent No. EP 1,157,718 (hereinafter "Street").

Whether claims 6–10 are unpatentable under 35 U.S.C. § 103(a) over Street in light of Hartley et al., U.S. Patent No. 6,161,042 (hereinafter "Hartley") and Bonnet, U.S. Patent No. 6,574,507 (hereinafter "Bonnet").

VII. ARGUMENT

Applicants respectfully traverse the rejection of claims 1–13 and request that this Appeal be sustained in its entirety.

A. The Section 112, First Paragraph Rejections of Claims 1–13

Claims 1–13 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking a written description with respect to treatment of "a detected apnea or hypopnea" (Final Action at 2).

1. The Section 112, Paragraph 1 Written Description Requirement

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. Am. Airlines, Inc., 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); In re Gosteli, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed.Cir. 1989)("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.")

Important here is that the specification need only "contain an equivalent description of . . . claimed subject matter." Lockwood, 107 F.3d at 1572, 41 U.S.P.Q.2d at 1966. Claimed subject matter need not be described in haec verba to satisfy the requirement. In re Smith, 481 F.2d 910, 914 (C.C.P.A. 1973); Lockwood, 107 F.3d at 1572, 41 U.S.P.Q.2d at 1966. An inherent disclosure is sufficient, provided that any missing descriptive matter is "present in the . . . specification such that one skilled in the art would recognize such a disclosure." In re Smith, 481 F.3d at 914.

2. Claim 1

Claim 1 recites:

> 1. An active implantable medical device comprising:
>
> means for measuring respiratory activity having an output signal representative of ventilatory activity of the patient;
>
> means for analyzing the ventilatory activity signal and detecting an occurrence of a respiratory apnea and an occurrence of a respiratory hypopnea;
>
> means for measuring a hemodynamic state having an output hemodynamic signal representative of the contractility of the myocardium, means for analyzing the hemodynamic signal and detecting an occurrence of a variation of the contractility;
>
> means for determining whether the detected contractility variation is significant; and
>
> means for conditionally modifying an operating parameter of the device **to treat a detected apnea or hypopnea** when said detected contractility variation is significant.

U.S. Patent Application No. 10/693,833 cl. 1 (emphasis added). The only claimed matter alleged by the Examiner to be lacking section 112, paragraph 1 written description support is the phrase "to treat a detected apnea or hypopnea." (Final Action at 2.) All of claims 1–13 will stand or fall together with respect to the written description rejection because all of the dependent claims 2–13 necessarily include this same limitation. Because this limitation is sufficiently described in the specification, the rejection for lack of written description should be reversed with respect to all of claims 1–13.

3. The Specification

The Specification states, in relevant part:

> The starting point of this invention lies in the observation by the inventors that a **systematic increase of the heart rate** in response to a detection of **apnea or hypopnea** is **not always a suitable *treatment***. Indeed, it has been reported that for certain patients the apnea or hypopnea could be followed by an adrenergic reaction. Such a reaction naturally induces a light tachycardia and a significant increase in blood pressure, sufficient to compensate for the fall of the ventilatory

activity. Among these patients, the myocardium thus can react naturally by adapting its contractility so as to increase the blood flow. In this way, the myocardium maintains the blood appreciably at the same level of oxygen saturation.

Ideally, to decide whether or not it is necessary to apply to the myocardium a stimulation at a frequency higher than the natural sinusal rate/rhythm of the patient, the best criterion would be a direct measurement of oxygen saturation in blood. Then, the stimulation would be started only in the event of a proven and significant desaturation. But such a direct measurement of oxygen saturation is difficult to implement in a simple and permanent manner in the context of an active implanted medical device, given the current state of the art.

Objects and Summary of the Invention

Broadly, the present invention proposes to overcome **the aforementioned deficiency in the *treatment* of the apnea and the hypopnea** by estimating variation of contractility of the myocardium by use of an hemodynamic sensor. Thus, in the event of a detected anomaly in the respiratory activity (i.e., **an apnea or hypopnea**), **before taking any therapeutic action**, the device estimates whether or not there was a correlative modification of the myocardium contractility.

1. If the hemodynamic sensor indicates the occurrence of a notable hemodynamic fall, revealing that the myocardium could not naturally adapt its contractility following the anomaly, or did not adapt sufficiently, **then the device takes an action in order to compensate for the oxygen desaturation induced by the respiratory disorder**. For example, if the hemodynamic fall and associated inadequate myocardium contractility follows an apnea or an hypopnea, then **a stimulation is triggered at a frequency that is higher than the natural sinusal rate/rhythm**.

(Specification at 2–3) (emphasis added). A person of ordinary skill in the art would understand from reading at least the above-quoted portion of Applicants' specification that there is an unambiguous written description to treat apnea (i.e., a SAS or Sleep Apnea Syndrome) and hypopnea. Specifically, Applicants disclosed in writing that "a systematic increase of the heart rate in response to a detection of an apnea or hypopnea is not always a suitable treatment," thereby telling persons skilled in the art that the invention disclosure is directed to a solution to this treatment problem, a more suitable "treatment" of such a detected apnea or hypopnea.

Further, the specification describes taking "therapeutic action" or an "action" (i.e., a treatment) in response to an apnea or hypopnea in combination with the significant contractility measure, to provide a suitable treatment of that detected apnea or hypopnea (Specification at 2). The specification goes on to explain that the "action" is taken "in order to compensate for the oxygen desaturation induced by the respiratory disorder" thereby treating the apnea or hypopnea, because, as the specification explains, "[t]he interruption or the reduction of the respiratory flow [i.e., apnea or hypopnea] involves a reduction in the oxygen concentration of blood (also known as the oxygen saturation)." (Id.) The treatment is specifically described as "a stimulation . . . triggered at a frequency that is higher than the natural sinusal rate/rhythm." (Id.)

Moreover as noted, the applicable law does not require that the claim language appear in haec verba in the specification to satisfy the written description requirement, although Applicants submit that it essentially is so found here, so long as there is equivalent or inherent disclosure, and would be so understood by a person of ordinary skill in the art.

In view of the foregoing, we respectfully submit that Applicants have provided a sufficient written description for the claimed subject matter and that the Examiner's rejections under section 112, paragraph 1 should be withdrawn.

B. The Section 102(b) Rejections of Claims 1–5 and 11–13

Claims 1–5 and 11–13 were rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Street.

"[A] claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." Celeritas Techs., Ltd. v. Rockwell Int'l. Corp., 150 F.3d 1354, 1361, 47 U.S.P.Q.2d 1516, 1522 (Fed. Cir. 1998). The standard for lack of novelty, that is, for "anticipation," is one of strict identity. Trintec Indus., Inc. v. Top-U.S.A. Corp., 295

F.3d 1292, 1296, 63 U.S.P.Q.2d 1597, 1600 (Fed. Cir. 2002).

Although the Examiner is correct that Street discloses an apparatus for monitoring periodic breathing as an indication of changes in the hemodynamic status of the heart, Street does not teach or suggest any functionality or structure for using the data acquired during monitoring to actually treat a detected apnea or hypopnea when said detected contractility variation is significant, as called for in claim 1. Rather, Street teaches to treat a different indication, namely, congestive heart failure, by ACE inhibitors, diuretics, digitalis, heart transplant, aerobic exercise or cardiac pacing. See Street [0006]–[0007]. Thus, because Street fails to disclose each and every element in claim 1, the Examiner's rejection should be withdrawn.

In addition, Street does not teach or suggest to use the combination of a detected apnea or hypopnea and a significant contractility variation to conditionally modify any operating parameter to treat the detected apnea or hypopnea, as required by claim 1. The Examiner correctly notes that Street teaches various techniques ("any of four physiologic parameters") to identify when a Periodic Breathing condition exists. A Periodic Breathing event can then be used—in an unexplained and non-enabled manner—"to recognize and facilitate the early termination of a developing exacerbation [citation omitted]" (Final Action at 3) of a cardiac insufficiency—i.e., congestive heart failure. However, nowhere does the Street reference disclose determining a contractility variation, let alone where it is a **significant** contractility variation, and the Examiner was unable to point to any such reference.

The Examiner referred to Street Fig. 2 as teaching "the contractility variation is analyzed before and after detection of hypopnea." We respectfully disagree. As we understand Street, a plain reading of the description of Fig. 2 demonstrates that what is depicted in Fig. 2 is no more

than determining whether a Periodic Breathing condition exists in a particular embodiment. Street [0029]–[0036]. Nowhere does Street teach or suggest to combine a detected apnea or hypopnea with a determined significant contractility variation to conditionally modify an operating parameter to treat a detected apnea or hypopnea. For this additional reason, the Examiner's rejection of claim 1 should be withdrawn.

Claims 2–13 depend from claim 1 and are allowable for at least the same reason that claim 1 is allowable. Accordingly, claims 2–13 also should be allowed.

C. The Section 103(a) Rejections of Claims 6–10

Dependent claims 6–7 were rejected under 35 U.S.C. § 103(a) as being rendered obvious by Street in view of Hartley; dependent claim 8 was rejected under 35 U.S.C. § 103(a) as being rendered obvious by Street in view of Bonnet; and dependent claims 9–10 were rejected under 35 U.S.C. § 103(a) as being rendered obvious by Street.

To establish a prima facie case of obviousness, there must be: (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine references teachings; (2) a reasonable expectation of success; and (3) prior art references which teach or suggest all of the claim limitations. See In re Kotzab, 217 F.3d 1365, 1370 (Fed. Cir. 2000); MPEP § 2143 (8th Ed., Rev. 1). As discussed above, Street fails to disclose the means element found in independent claim 1 for "conditionally modifying an operating parameter of the device to treat a detected apnea or hypopnea when said detected contractility variation is significant." Moreover, Bonnet and Hartley, the secondary references cited by the Examiner in this Office action, both fail to disclose this feature, and thus do not cure the deficiency of the primary reference. Thus,

Street, when considered alone or in combination with either Bonnet or Hartley, or both, fails to disclose all the elements taught in amended claim 1.

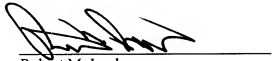
Furthermore, none of the references would motivate one to modify any of the other references to include this functionality. Although Street discloses monitoring periodic breathing, none of the references disclose any means for applying a therapy to treat the apnea or hypopnea as claimed in claim 1. Indeed, Hartley discloses a rate adaptive cardiac rhythm management device that fails to address the issue of periodic breathing. Bonnet discloses a method for treating apneas, but fails to disclose any method or functionality for detecting and treating hypopneas. And, as discussed above, Street only discloses an apparatus and method for monitoring periodic breathing and fails to disclose any functionality or structure for applying a therapy when changes are detected. Here, the prior art references, even when combined, and we submit that there is no proper basis to combine them, provide no suggestion of desirability in making the combination as evidenced by their failure to disclose all of the elements taught in amended claim 1.

C. CONCLUSION

Applicants respectfully submit that, in view of the foregoing, they have made a patentable contribution to the art. It is respectfully requested that the Board reverse the Examiner on the issues presented on appeal in this Brief and withdraw the rejections of claims 1–13.

Date: August 14, 2008

Respectfully submitted,



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CLAIMS APPENDIX

I. Claims Involved in This Appeal

1. An active implantable medical device comprising:

means for measuring respiratory activity having an output signal representative of ventilatory activity of the patient;

means for analyzing the ventilatory activity signal and detecting an occurrence of a respiratory apnea and an occurrence of a respiratory hypopnea;

means for measuring a hemodynamic state having an output hemodynamic signal representative of the contractility of the myocardium, means for analyzing the hemodynamic signal and detecting an occurrence of a variation of the contractility;

means for determining whether the detected contractility variation is significant; and

means for conditionally modifying an operating parameter of the device to treat a detected apnea or hypopnea when said detected contractility variation is significant.

2. The device of claim 1, wherein means for determining whether the contractility variation is significant further comprises means for operating said analyzing means to analyze said hemodynamic signal detected after detection of said apnea or hypopnea.

3. The device of claim 1, wherein the means for determining whether the contractility variation is significant further comprises means for operating said analyzing means to analyze said hemodynamic signal detected before detection of said apnea or hypopnea.

4. The device of claim 1, wherein the hemodynamic measuring means further comprises means for measuring an intracardiac impedance.

5. The device of claim 1, wherein the hemodynamic measuring means further comprises means for measuring an endocardial acceleration.

6. The device of claim 1, wherein said operating parameter has a first value and said conditionally modifying means further comprises means for modifying in a temporary manner said operating parameter to a second value different from said first value.

7. The device of claim 6, wherein said conditionally modifying means further comprises means for restoring said operating parameter to said first value in response to said hemodynamic signal analysis means no longer detecting a variation of myocardium contractility.

8. The device of claim 1, wherein said operating parameter is a stimulation frequency, and said conditional modification is an increase in response to a detected significant variation and a detected apnea or hypopnea.

9. The device of claim 1, wherein said operating parameter is an atrio-ventricular delay and said conditional modification is a shortened delay in relation to a detected significant variation and a detected apnea or hypopnea.

10. The device of claim 1, wherein said device further comprises means for stimulating a patient's heart having at least a first stimulation mode for delivering a multisite stimulation, wherein said operating parameter is a mode of cardiac stimulation, and said conditional modification comprises means for operating said stimulation means to trigger a multisite stimulation in relation to said detected significant variation and a detected apnea or hypopnea.

11. The device of claim 2, wherein the hemodynamic signal analyzing means further comprises means for comparing a first hemodynamic signal measured during a cardiac cycle following the respiratory cycle during which the apnea or hypopnea was detected, with an average of the hemodynamic signals acquired prior to said respiratory cycle.

12. The device of claim 2, wherein the hemodynamic signal analyzing means further

comprises means for comparing a first hemodynamic signal measured after a plurality of cardiac cycles following the respiratory cycle during which the apnea or hypopnea was detected with an average of the hemodynamic signals acquired prior to said respiratory cycle during which the apnea or hypopnea was detected.

13. The device of claim 1, wherein said device further comprises means for comparing a detected contractility variation to a reference threshold, and determining a significant variation in response to said contractility variation being greater than said threshold.

EVIDENCE APPENDIX

1. Street et al., European Patent No. EP 1,157,718.

2. Hartley et al., U.S. Patent No. 6,161,042.

3. Bonnet, U.S. Patent No. 6,574,507.

APPENDIX #1

EP Patent No. 1,157,718 A2

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(11) EP 1 157 718 A2

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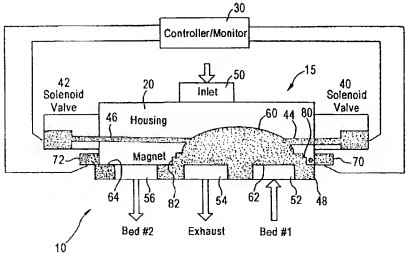
(54) Linear gas valve cycle control, shut-off-valve and self test

(57) A control system for controlling a gas generating system including at least two molecular sieve beds comprises a linear valve having a housing which includes an inlet connected to the gas generating system, a first port connected to a first of the at least two molecular sieve beds, a second port for exhaust, and a third port connected to a second of the at least two molecular sieve beds. Said inlet and said first, second and third parts are all in communication with a slide chamber having a slide block positioned in said slide chamber. The control system further comprises a push-pull device which is mounted to said housing for moving said slide block in a first direction and in a second direction, a sensor positioned at opposite ends of said slide chamber for sensing the position of said slide block in said slide chamber, and a controller for receiving information from said sensing device and for controlling said push-pull device.

FIG. 1



EP 1 157 718 A2

Description

Field of the Invention

[0001] The present invention relates generally to gas valves, and more particularly, to a linear gas valve in which the position of a slide block housed therein can be detected.

Background of the Invention

[0002] On Board Inert Gas Generating Systems (OBIGGS) or On Board Oxygen Generating Systems (OBOGS) utilize molecular sieve by employing a pressure swing adsorption (PSA) process that has been used for many years to generate either nitrogen or oxygen product sequentially, respectively. This process of sequential pressurization and venting is the PSA process. This PSA technology uses conditioned engine bleed air fed through the valve to pressurize molecular sieve contained in each of a number of canisters. After a predetermined period of time, a valve changes state, venting the one pressurized canister and then pressurizing the next canister. Previous PSA systems have been controlled by a rotary valve which is controlled by a valve and driven by a fixed or variable speed motor.

[0003] Recent PSA systems utilize a linear 4-way slide valve, which connects, input air with one canister, while connecting a vent port with another canister. The valve changes state, which connects the vent port with the first canister and simultaneously connecting the second canister with the input air.

[0004] The linear valve used on typical PSA systems is pneumatically operated using control pilot gas from miniature pilot solenoid valves and are opened and closed using solid state electronics which are housed in an EMI shielded enclosure. The pilot solenoids provide gas pressure to two gas cylinders, which are connected to a sliding block. The block slides across a mating plate with three openings or ports. The ports are constructed in a straight line. The outer ports are equal-distance from center port. The sliding block has an undercut, which acts as a flow path. The flow path is sized to connect two of the three ports at any one point in time. A controller is set to open and close the miniature pilot valves at a predetermined time or "cycle time".

[0005] The PSA device functions by forcing the undesired gas molecules into "sites" in the molecular sieve. The cycle time of the PSA process is largely determined by what purity is desired of the product gas. Using the linear valve, the slide block is controlled to provide the air to the desired canister and simultaneously vent the other canister. If the slide block slows down the resulting purity changes

[0006] Airborne OBOGS systems usually have oxygen monitors to detect oxygen purity degradation and alarm the operator/pilot of a failure to produce desired oxygen. There are a number of internal and external conditions which result in poor oxygen. One internal condition which would cause poor purity would be a slide valve, which did not change state or changed state slower than desired. Airborne OBIGGS systems do not have nitrogen monitors. Some systems use an oxygen monitor and infer the nitrogen purity from the amount of residual oxygen in the product system. Nitrogen product purity is affected in the same manner as oxygen product purity if the slide valve fails to operate properly External conditions which cause oxygen purity degradation include ambient temperature, below normal operating pressure, sieve degradation, moisture, etc.

[0007] The PSA process handles moisture entrained in the air during normal operation. If moisture enters the system through the air system, when the PSA process is not operating, the result is permanent damage to the molecular sieve. Damaged sieve does not separate air. Many OBOGS and OBIGGS systems have separate shut-off valves which prevent the entrance of air into the molecular sieve beds when the system is not operating. Thus, a need exists in the art for a linear valve having a slide block in which the current position of the slide block can be detected. Another need exists for a linear valve in which the separate shut-off valve is eliminated.

Summary of the Invention

[0008] It is, therefore, an object of the present invention to provide a linear valve and control system in which the location of the slide block is monitored to trouble shoot performance problems before they occur.

[0009] Another object of the present invention is to provide a linear valve having a slide block in which the position is monitored by a sensing device.

[0010] Another object of the present invention is to provide a linear valve in which a shutoff valve is eliminated between the linear valve and an air source.

[0011] The present invention relates to detecting the state of a slide block positioned in a linear valve and using the position of the slide block to predict the health of a linear valve and provide information to a controller/monitor. An operator is provided with information before failure occurrence to allow preventative maintenance of the linear valve.

[0012] The linear valve is constructed with two canister ports and a vent port. The slide block can be constructed to block the two canister ports and vent port simultaneously. The system can control the position of the block, when provided with position information, hence, using the slide block as a shutoff valve. The typical slide valve can be used as an integral slide shutoff valve, reducing system complexity and reducing system weight, which is critical to airborne applications.

[0013] These and other objects of the present invention are achieved by a control system for controlling a gas generating system including at least two molecular sieve beds. A linear valve has a housing including an inlet connected to the gas generating system and a first

port connected to a first of the at least two molecular sieve beds, a second port for exhaust, and a third port connected to a second of the at least two molecular sieve beds. The inlet, the first, second and third ports are all in communication with a slide chamber in the housing. A slide block is positioned in the slide chamber. A push-pull device is mounted to the housing for moving the slide block in a first direction and in a second direction. A sensor is positioned at opposite ends of the slide chamber for sensing the position of the slide block in the slide chamber. A controller is provided for receiving information from the sensing device and for controlling the push-pull device.

[0014] The foregoing and other objects of the present invention are also achieved by a linear valve including a housing. The housing includes an inlet connected to a gas generating system and a first port connected to a first of at least two molecular sieve beds, a second port for exhaust, and a third port connected to a second of the at least two molecular sieve beds, with the inlet, the first, second and third ports all in communication with a slide chamber in the housing with a slide block positioned in the slide chamber. A push-pull device is mounted to the housing for moving the slide block in a first direction and in a second direction. A sensor is positioned at opposite ends of the slide chamber for sensing the position of the slide block in the slide chamber.

[0015] The foregoing and other objects of the present invention are also achieved by a method of monitoring an operational status of a linear valve including detecting when a linear slide block is in one of at least two positions, determining at least one of slew rate, full length stroke and uneven stroke and alerting a user if one of the slew rate, full length stroke and uneven stroke exceeds a predetermined value.

[0016] Still other objects and advantages of the present invention will become readily apparent to those skilled in the art from the following detailed description, wherein the preferred embodiments of the invention are shown and described, simply by way of illustration of the best mode contemplated of carrying out the invention. As will be realized, the invention is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, all without departing from the invention. Accordingly, the drawings and description thereof are to be regarded as illustrative in nature, and not as restrictive.

Brief Description of the Drawings

[0017] The present invention is illustrated by way of example and not by limitation, in the figures of the accompanying drawings, wherein elements having the same reference numeral designations represent like elements throughout and wherein:

Figure 1 is a schematic illustration of a linear valve including a slide block and a sensing device for sensing the current location of the slide block in the valve housing;

Figure 2 is a drawing similar to Figure 1 with the slide block shown in a second position;

Figure 3 is an alternative embodiment similar to Figures 1 and 2 using air cylinders to drive the slide block;

Figure 4 is another embodiment in which the linear valve housing is made large enough that the slide block can be moved to a position in which all three ports are blocked; and

Figure 5 is a pneumatic circuit diagram illustrating the pneumatic circuit used in the embodiment depicted in Figure 3.

Figure 6 is a top level block diagram of a pneumatic circuit.

Best Mode for Carrying Out the Invention

[0018] Referring to Figure 1, a linear slide valve system, generally indicated at 10, includes a linear slide valve assembly 15 and a controller/monitor 30 according to the present invention. Linear valve assembly 15 includes a pair of solenoid valves 40, 42 mounted on opposite ends of a housing 20. The housing 20 includes an inlet 50 on one side of the housing 20, a first port 52, second port 54 and a third port 56, all on an opposite side of the housing 20. The ports 52, 54, 56 are provided in the base plate 48. Ports 52 and 56 are equally spaced from the central port 54. A slide block 60 includes a flat surface 62 sliding on an upper surface 64 of the plate 48. In the embodiment depicted in FIgure 1, the inlet 50 is spaced from the slide block 60 and the slide block 60 is of sufficient length to cover either ports 52, 54 or ports 54, 56. The solenoids 40, 42 are 3-way solenoids of the type known in the art and are utilized in a preferred embodiment of the invention. Other control means, solenoid, air or otherwise can be used without departing from the spirit and scope of the invention.

[0019] The slide block 60 is driven in a first direction by solenoid valve 40 and in an opposite direction or second direction by solenoid valve 42. Rods 44 and 46 are attached to solenoid valves 40, 42 and to the sliding block to move the sliding block in opposite directions. Proximity switches 70, 72 are mounted on opposite ends of housing 20. On opposite sides of slide block 60 are mounted a pair of magnets 80, 82 which when brought into proximity with switches 70, 72, respectively, a signal is sent to the controller/monitor 30 as will be described in greater detail below. As depicted in Figure 1, the slide block 60 is shown in a first position blocking ports 52 and 54. In this manner, inlet 50 is in communication with port 56 to bed # 2. In this first position, bed #1 can exhaust through the port 52 through the slide block 60 into the exhaust port 54 while air is provided from the inlet 50 through the port 56 to bed #2.

[0020] Figure 2 is similar to Figure 1 except that the slide block is depicted in a second position. In this sec-

ond position, bed #2 can exhaust through the port 56 and through the slide block 60 into the exhaust port 54 while air is provided from the inlet 50 through the port 52 to bed #1. Generally a spring (not shown) is used between the piston and the slide block 60. Closed cell foam has also been used. The valve located in Figure 2 does not have a spring or foam. Instead the valve has tight tolerances with the assembly to maintain position of the slide valve. The valve will become seal tight under operating pressures.

[0021] Figure 3 is similar to the embodiment depicted in Figures 1 and 2 except that instead of solenoid valves 40, 42, a pair of air cylinders 140, 142 are used to move a driving member 150 in a first and second direction. The driving member 150 is an elongated cylindrically shaped member having two intermediate shoulder members 152, 154 and two piston heads 162, 164. The two intermediate shoulders are partially positioned in slots 166, 168, respectively for engagement with a sliding block 160. The sliding block 160 includes magnets 80, 82 mounted in the lower surface 64. A pair of sensors 70, 72 are mounted in the plate 48 at opposite ends of a slide block chamber 170. Formed between the piston heads 160, 162 and plate 48 is the slide block chamber 170. An inlet (not shown) is centered in the housing just above the exhaust port. At opposite ends of housing 120 are opposite cylindrical bores 180, 182, in which piston heads 160, 162 slide in a reciprocal fashion, respectively. Threaded on opposite surfaces of housing 120 are threads and onto each of the threads are caps 190, 192 to seal off and form a first cylinder 200 and a second cylinder 202 in which piston heads 160, 162 slide respectively. Poppets 210, 212 are located in threaded members 190, 192. The driving member 150 is moved in opposite directions as follows. As depicted in Figure 3, poppet 210 would be opened and the cylinder 200 pressurized while poppet 212 would also be opened allowing the cylinder to be vented thereby moving the driving member to the right with the cylinder 202 being vented. Figure 3 also best depicts an undercut 169 through the slide block 160 which permits flow between ports 52, 54 while sealing these ports from the slide chamber 170.

[0022] Although proximity sensors and magnetic sensors have been described, it should be understood that other sensors could be used in the present invention in any of the embodiments described herein. Optical sensors have become very popular recently with infra red and laser. These devices can be very precise. These devices can detect the range of travel as well as the limits of travel. The exact location of the sliding block 60, 160 could be known at all times.

[0023] Pressure transducers are commonly used in testing for such information as cycle rates and slide valve operation by monitoring the cylinder pressure. In conjunction with a strip chart, the operating pressure can be determined pretty accurately. This device can be used to determine the approximate location of the slide block (will not locate precisely).

[0024] Contacts could be placed on the end of the sliding block 60, 160 and in the housing at the end of its travel. This would indicate whether the block was completing its stroke and the time it takes to get there. This device would be the simplest to incorporate and would be very accurate in time of piston travel and piston location and is considered the presently preferred embodiment.

[0025] The slide valve depicted in Figure 4 is similar to the linear slide valves depicted in Figures 1-3 except that the slide chamber 470 has greater length to enable a slide block 460 to be able to simultaneously cover ports 52, 54, 56. The sensors are located in the same position as those in Figure 1 with the possible addition of another located centered on the slides of the slide block. This would enable the detection of the slide block in the shut off position. Advantageously, in this embodiment, the shut-off valve 600 (Figure 6) can be eliminated. In the slide chamber 470 depicted in Figure 4, there is greater spacing between the ports 52 and 56 and ends of the slide chamber to allow the slide block 460 to move to the first and second positions depicted in dashed lines in Figure 4.

[0026] Figure 5 depicts a schematic for operating the linear slide valve depicted in Figure 3. In Figure 5, the proximity switches 70, 72 are depicted as connected to the controller/monitor 30. Three way valves 500, 502 are also each connected to the controller/monitor 30 and are pneumatically connected to the air cylinders 200, 202. As valve 500 is in a first position inlet air is introduced into the cylinder 202, thereby forcing the piston 164 to change position which triggers the proximity switch 70 to open and the proximity switch 72 to close. One way of monitoring the health of the slide valve 15 might be as follows: The controller/monitor commands the slide valve 15 to switch to the opposite of its two positions. As soon as the proximity switch 70, 72 (sensing the current position) senses that the slide block 60 has begun to move from the first position, a timer in the controller/monitor 30 is started. When the controller/monitor 30 receives the signal from the sensor 70, 72 that the slide block 60 has reached the opposite position, the timer is stopped. The length of time elapsed is a measure of the transition time for the valve 15. The controller/monitor 30 can detect conditions that have effects on the travel time of the valve 15 such as input air pressure and temperature. Comparing this time to an acceptable time (for the known input pressure and temperature conditions) provides a measure of the performance of the valve. A simple display can show instantaneous cycle rate, which could be monitored or a signal would light when cycles rate become out of tolerance. In the case of using the slide block 60 as a shut off valve, the controller/monitor 30 would be used to control the position of the slide block 60 from the location information supplied by the sensors 70, 72. It should now be understood that a linear valve and control system has been described in which the location of the slide block is monitored to trouble-

shoot performance before they occur. It should also be apparent that a linear valve has been described which eliminates the shut-off valve.

[0027] It will be readily seen by one of ordinary skill in the art that the present invention fulfils all of the objects set forth above. After reading the foregoing specification, one of ordinary skill will be able to affect various changes, substitutions of equivalents and various other aspects of the invention as broadly disclosed herein. It is therefore intended that the protection granted hereon be limited only by the definition contained in the appended claims and equivalents thereof.

Claims

1. A control system for controlling a gas generating system including at least two molecular sieve beds, comprising:

   a linear valve having a housing including an inlet connected to the gas generating system and a first port connected to a first of the at least two molecular sieve beds, a second port for exhaust, and a third port connected to a second of the at least two molecular sieve beds, with said inlet, said first, second and third ports all in communication with a slide chamber having a slide block positioned in said slide chamber;
   a push-pull device is mounted to said housing for moving said slide block in a first direction and in a second direction;
   a sensor positioned at opposite ends of said slide chamber for sensing the position of said slide block in said slide chamber; and
   a controller for receiving information from said sensing device and for controlling said push-pull device.

2. The system of claim 1, wherein said sensing device is one of an optical sensor, a pressure transducer, a magnetic switch and a contact switch.

3. The system of claim 1, wherein said sensor is a magnetic switch and wherein a plurality of magnets mounted to said sliding block and a corresponding plurality of proximity switches mounted to said housing.

4. The system of claim 1, wherein said sliding block has a first position in which port said sliding block covers said first port and said second port such that the gas generating system can provide product gas through said inlet and said third port to the second of the molecular sieve beds and the first molecular sieve bed can be vented through said first port to said second port and a second position in which said sliding block covers said third port and said second port such that the gas generating can provide product gas through said inlet and said first port to the first of the molecular sieve beds and the second molecular sieve bed can be vented through said third port to said second port.

5. The system of claim 4, wherein said slide block includes a flow path.

6. The system of claim 1, wherein the gas generating system is an oxygen concentrator.

7. The system of claim 1, wherein said controller monitors the current location of said slide block during operation and determines slew rate, full-length stroke and uneven stroke.

8. The system of claim 1, wherein said push-pull device is one of a pair of air cylinders and a pair of solenoid valves.

9. The system of claim 6, wherein said oxygen concentrator uses pressure swing adsorption.

10. The system of claim 4, wherein said sliding block has a third position covering said first port, said second port and said third port.

11. The system of claim 1, further comprising an oxygen monitor for monitoring the quality of gas provided to said first port and said second port by the gas generating system.

12. A linear valve, comprising:

    a housing including an inlet connected to a gas generating system and a first port connected to a first of at least two molecular sieve beds, a second port for exhaust, and a third port connected to a second of the at least two molecular sieve beds, with said inlet, said first, second and third ports all in communication with a slide chamber in the housing with a slide block positioned in said slide chamber,
    a push-pull device is mounted to said housing for moving said slide block in a first direction and in a second direction; and
    a sensor positioned at opposite ends of said slide chamber for sensing the position of said slide block in said slide chamber.

13. The linear valve of claim 12, wherein said sensing device is one of an optical sensor, a pressure transducer, a magnetic switch and a contact switch.

14. The linear valve of claim 12, wherein said sensor is a magnetic switch and wherein a plurality of magnets mounted to said sliding block and a corre-

sponding plurality of proximity switches mounted to said housing.

15. The linear valve of claim 12, wherein said sliding block has a first position in which port said sliding block covers said first port and said second port such that the gas generating system can provide product gas through said inlet and said third port to the second of the molecular sieve beds and the first molecular sieve bed can be vented through said first port to said second port and a second position in which said sliding block covers said third port and said second port such that the gas generating can provide product gas through said inlet and said first port to the first of the molecular sieve beds and the second molecular sieve bed can be vented through said third port to said second port.

16. The linear valve of claim 12, wherein said slide block includes a flow path.

17. The linear valve of claim 12, wherein the gas generating system is an oxygen concentrator.

18. The linear valve of claim 12, wherein said controller monitors the current location of said slide block during operation and determines slew rate, full-length stroke and uneven stroke.

19. The linear valve of claim 12, wherein said push-pull device is one of a pair of air cylinders and a pair of solenoid valves.

20. The linear valve of claim 12, wherein said oxygen concentrator uses pressure swing adsorption.

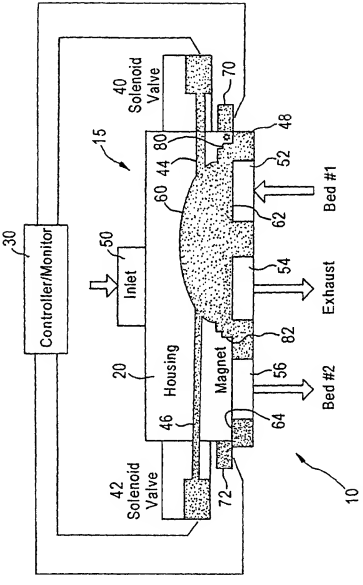
21. The linear valve of claim 12, wherein said sliding block has a third position covering said first port, said second port and said third port.

22. The linear valve of claim 12, further comprising an oxygen monitor for monitoring the quality of gas provided to said first port and said second port by the gas generating system.

23. A method of monitoring an operational status of a linear valve, comprising:

detecting when a linear slide block is in one at least two positions;
determining at least one of slew rate, full length stroke and uneven stroke; and
alerting a user if one of the slew rate, full length stroke and uneven stroke exceeds a predetermined value.

FIG. 1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Controller/Monitor
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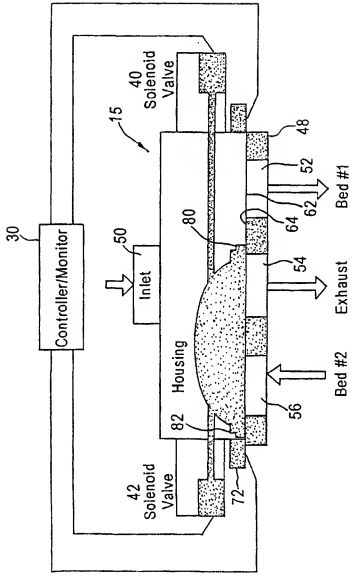
Solenoid
Valve
70
15
48
80
44
52
60
62
Bed #1
50
Inlet
54
Exhaust
20
Housing
Magnet
82
56
46
64
Bed #2
42
Solenoid
Valve
72
10

FIG. 2


30
Controller/Monitor
40
Solenoid
Valve
15
48
52
Bed #1
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Inlet
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Exhaust
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Bed #2
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82
42
Solenoid
Valve
72

FIG. 3

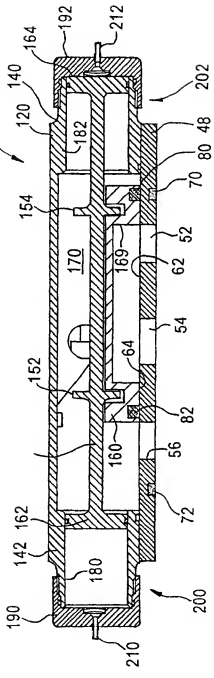
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FIG. 4

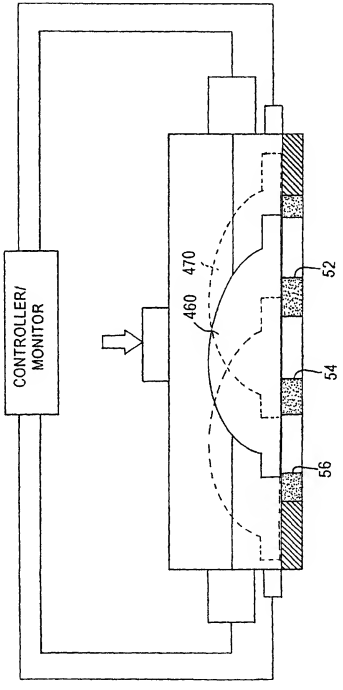
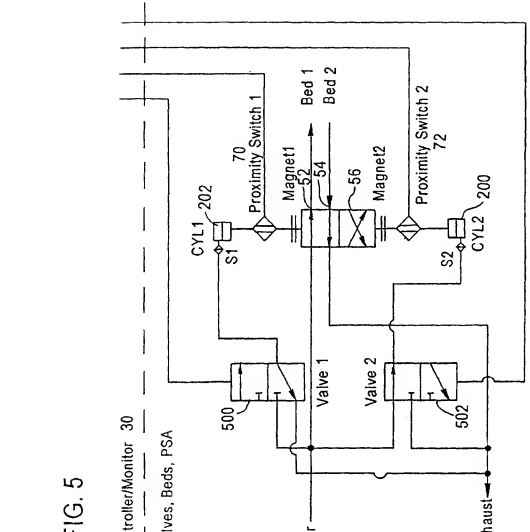


FIG. 5



Note: As valve 1 pressurizes cylinder 1, the piston changes position, which triggers proximity switch 1 to open and proximity switch 2 to close.

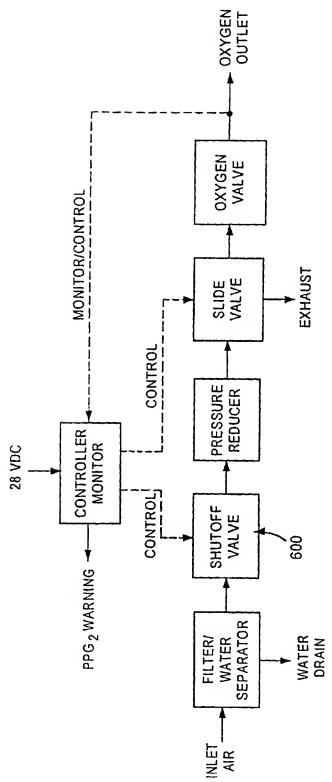

INLET AIR
FILTER/ WATER SEPARATOR
WATER DRAIN
SHUTOFF VALVE
600
PRESSURE REDUCER
SLIDE VALVE
EXHAUST
OXYGEN VALVE
OXYGEN OUTLET
CONTROL
CONTROL
MONITOR/CONTROL
28 VDC
CONTROLLER MONITOR
PPG2 WARNING

FIG. 6

APPENDIX #2

US Patent No. 6,161,042

US006161042A

United States Patent [19]

Hartley et al.

[11] Patent Number: 6,161,042

[45] Date of Patent: Dec. 12, 2000

[54] **RATE ADAPTIVE CARDIAC RHYTHM MANAGEMENT DEVICE USING TRANSTHORACIC IMPEDANCE**

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[21] Appl. No.: **09/316,690**

[22] Filed: **May 21, 1999**

Related U.S. Application Data

[62] Division of application No. 09/032,731, Feb. 27, 1998, Pat. No. 6,076,015.

[51] **Int. Cl.**[7] **A61N 1/365**

[52] **U.S. Cl.** **607/20**; 607/28; 600/547

[58] **Field of Search** 607/9, 17, 20, 607/28; 600/547

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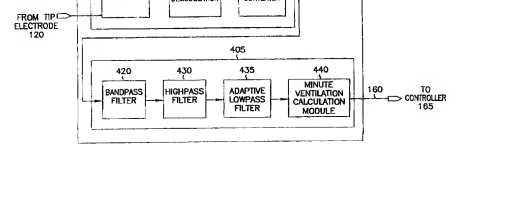
Primary Examiner—Kennedy Schaetzle

Attorney, Agent, or Firm—Schwegman, Lundberg, Woessner & Kluth, P.A.

[57] **ABSTRACT**

A cardiac rhythm management (CRM) device detects transthoracic impedance, extracts ventilation or other information, and adjusts a delivery rate of the CRM therapy accordingly. A four-phase sequence of alternating direction current pulse stimuli is periodically delivered to a patient's thorax. A transthoracic impedance signal is extracted using a weighted demodulation. Signal processing extracts ventilation information and removes cardiac stroke information using an adaptive lowpass filter. The adaptive filter cutoff frequency is based on the patient's heart rate; a higher cutoff frequency is provided for higher heart rates. Peak/valley detection indicates tidal volume, which is integrated to extract minute ventilation (MV). Short and long term averages are formed and compared to establish a MV indicated rate. Rate adjustment ignores MV information when a noise-measurement exceeds a threshold. An interference avoidance circuit delays delivery of the stimuli when telemetry pulses or other interfering signals are detected.

45 Claims, 10 Drawing Sheets



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5,379,776	1/1995	Murphy et al.	128/705
5,391,190	2/1995	Pederson et al.	607/23
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5,441,524	8/1995	Rueter et al.	607/18
5,507,785	4/1996	Deno	607/24
5,524,632	6/1996	Stein et al.	128/733
5,562,711	10/1996	Yerich et al.	607/17
5,562,712	10/1996	Steinhaus et al.	607/20
5,626,622	5/1997	Cooper	607/18
5,800,470	9/1998	Stein et al.	607/20
5,817,135	10/1998	Cooper	607/17
5,817,136	10/1998	Nappholz	607/17
5,824,020	10/1998	Cooper	607/17
5,824,029	10/1998	Weijand et al. .	

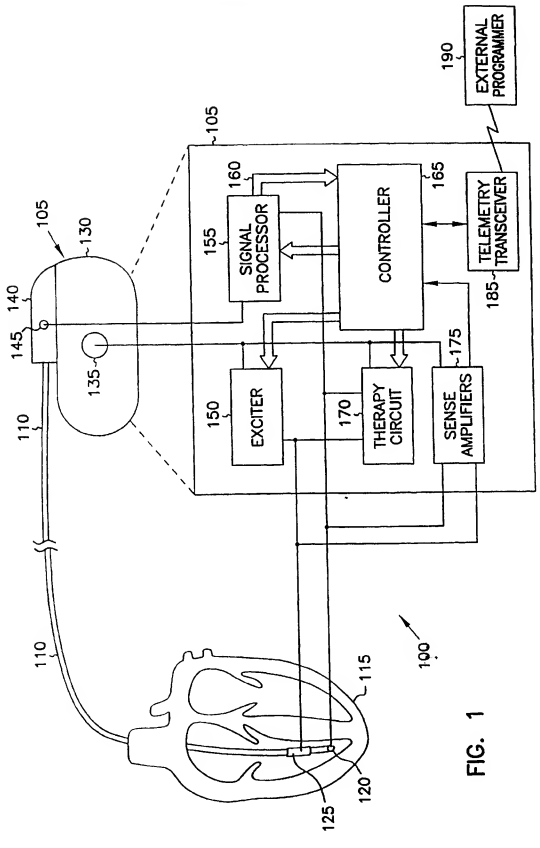
190
EXTERNAL PROGRAMMER
105
160
165
155
SIGNAL PROCESSOR
CONTROLLER
TELEMETRY TRANSCEIVER
185
105
130
140
145
135
175
150
EXCITER
170
THERAPY CIRCUIT
SENSE AMPLIFIERS
110
110
115
190
125
120

FIG. 1

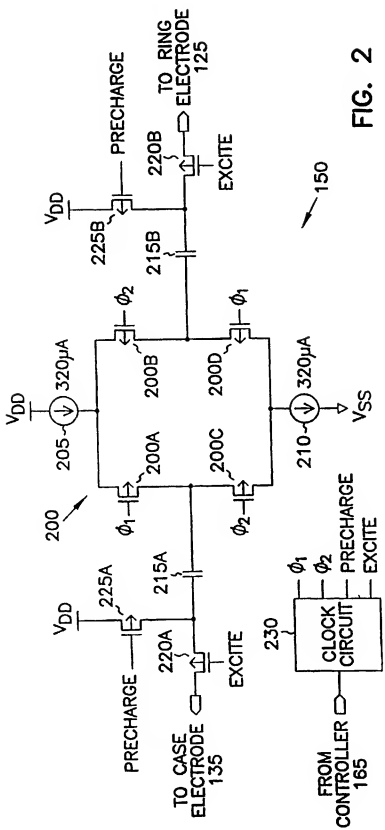
V_{DD}
320μA
205
200
200A
200B
200C
200D
ϕ_1
ϕ_2
210
320μA
V_{SS}
150
225A
215A
220A
PRECHARGE
EXCITE
TO CASE ELECTRODE 135
225B
215B
220B
PRECHARGE
EXCITE
TO RING ELECTRODE 125
230
CLOCK CIRCUIT
PRECHARGE
EXCITE
FROM CONTROLLER 165

FIG. 2

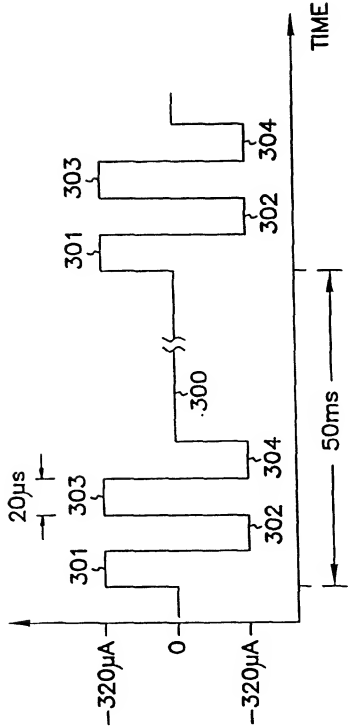
TIME
-320μA
0
-320μA
20μs
301
303
302
304
300
301
303
302
304
50ms

FIG. 3

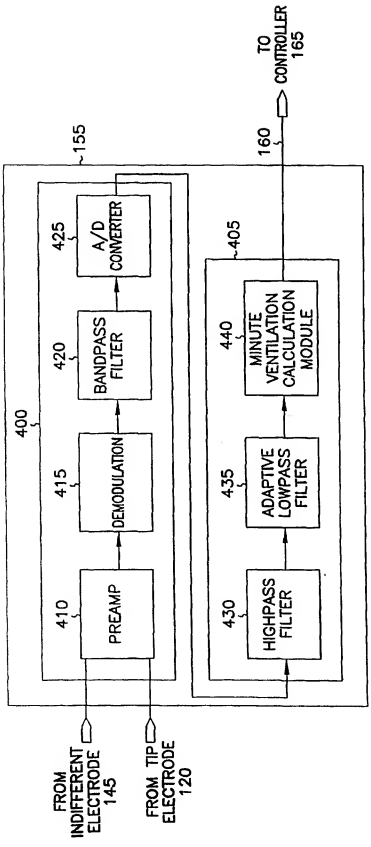
FROM INDIFFERENT ELECTRODE 145
FROM TIP ELECTRODE 120
400
410
PREAMP
415
DEMODULATION
420
BANDPASS FILTER
425
A/D CONVERTER
155
405
430
HIGHPASS FILTER
435
ADAPTIVE LOWPASS FILTER
440
MINUTE VENTILATION CALCULATION MODULE
160
TO CONTROLLER 165

FIG. 4

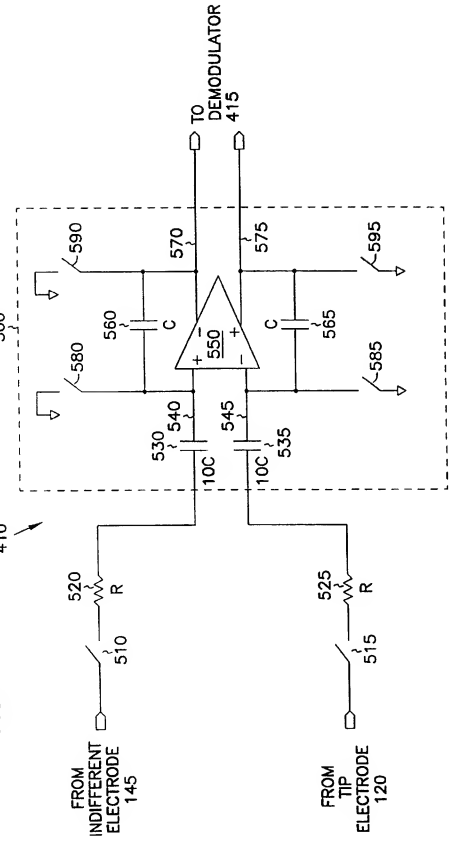
TO DEMODULATOR 415
500
590
570
575
595
560
C
550
C
565
580
585
540
545
530
535
10C
10C
410
520
R
525
R
510
515
FROM INDIFFERENT ELECTRODE 145
FROM TIP ELECTRODE 120

FIG. 5

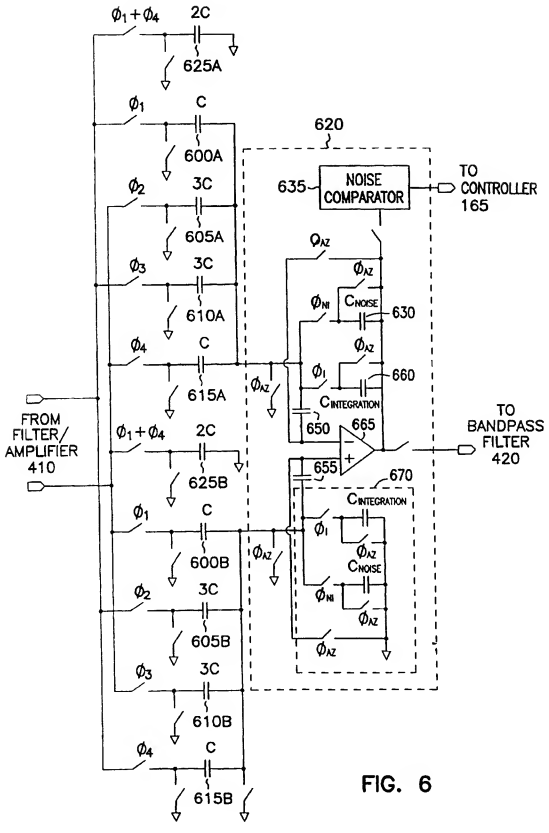
$\phi_1+\phi_4$
2C
625A
ϕ_1
C
600A
620
ϕ_2
3C
605A
635
NOISE COMPARATOR
TO CONTROLLER 165
ϕ_{XZ}
ϕ_3
3C
610A
ϕ_{NI}
C_{NOISE}
630
ϕ_4
C
615A
ϕ_I
660
$C_{INTEGRATION}$
650
665
FROM FILTER/ AMPLIFIER 410
$\phi_1+\phi_4$
2C
625B
TO BANDPASS FILTER 420
655
670
ϕ_1
C
600B
ϕ_2
3C
605B
ϕ_3
3C
610B
ϕ_4
C
615B

FIG. 6

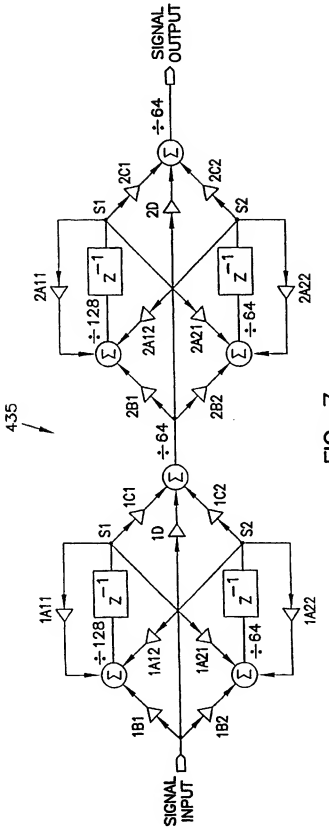
SIGNAL INPUT
SIGNAL OUTPUT
435
÷64
÷128
÷64
S1
S2
1A11
1A12
1A21
1A22
1B1
1B2
1C1
1C2
1D
2A11
2A12
2A21
2A22
2B1
2B2
2C1
2C2
2D
Z⁻¹

FIG. 7

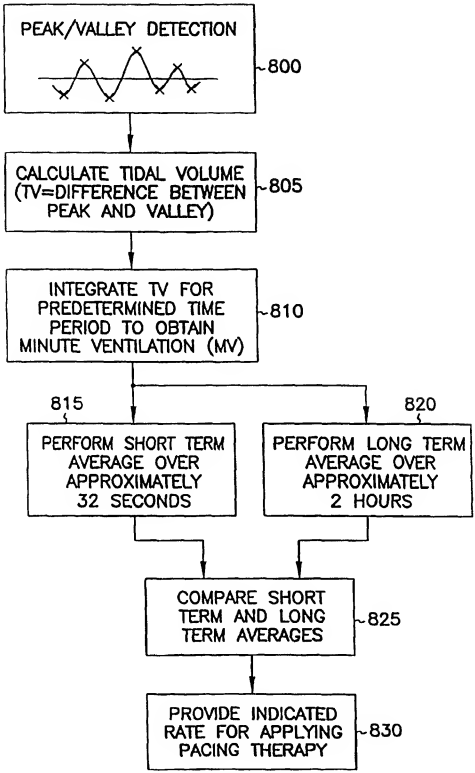
PEAK/VALLEY DETECTION
800
CALCULATE TIDAL VOLUME (TV=DIFFERENCE BETWEEN PEAK AND VALLEY)
805
INTEGRATE TV FOR PREDETERMINED TIME PERIOD TO OBTAIN MINUTE VENTILATION (MV)
810
815
PERFORM SHORT TERM AVERAGE OVER APPROXIMATELY 32 SECONDS
820
PERFORM LONG TERM AVERAGE OVER APPROXIMATELY 2 HOURS
COMPARE SHORT TERM AND LONG TERM AVERAGES
825
PROVIDE INDICATED RATE FOR APPLYING PACING THERAPY
830

FIG. 8

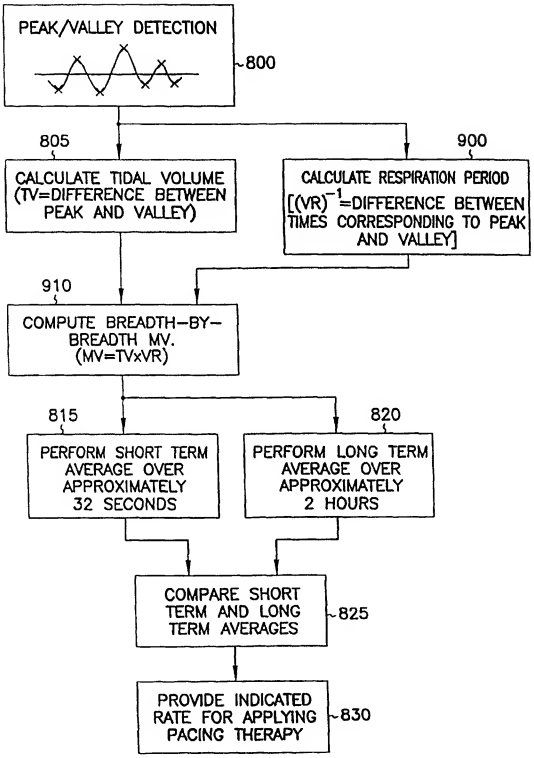
PEAK/VALLEY DETECTION
800
805
CALCULATE TIDAL VOLUME (TV=DIFFERENCE BETWEEN PEAK AND VALLEY)
900
CALCULATE RESPIRATION PERIOD [(VR)$^{-1}$=DIFFERENCE BETWEEN TIMES CORRESPONDING TO PEAK AND VALLEY]
910
COMPUTE BREADTH-BY-BREADTH MV. (MV=TVxVR)
815
PERFORM SHORT TERM AVERAGE OVER APPROXIMATELY 32 SECONDS
820
PERFORM LONG TERM AVERAGE OVER APPROXIMATELY 2 HOURS
COMPARE SHORT TERM AND LONG TERM AVERAGES
825
PROVIDE INDICATED RATE FOR APPLYING PACING THERAPY
830

FIG. 9

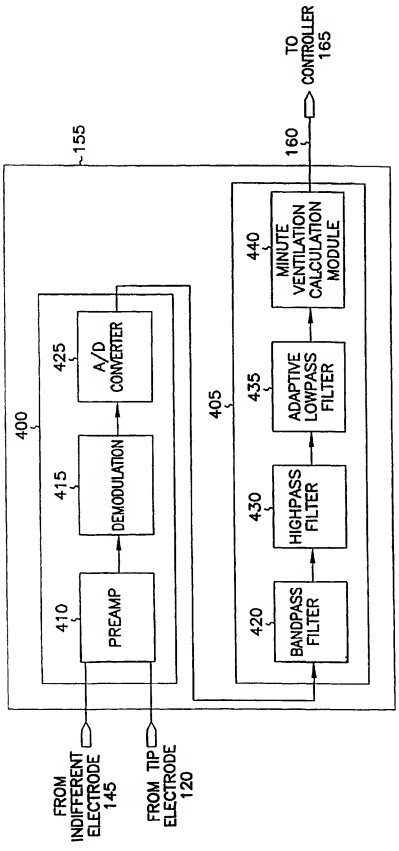
FROM INDIFFERENT ELECTRODE 145
FROM TIP ELECTRODE 120
155
400
410
PREAMP
415
DEMODULATION
425
A/D CONVERTER
405
420
BANDPASS FILTER
430
HIGHPASS FILTER
435
ADAPTIVE LOWPASS FILTER
440
MINUTE VENTILATION CALCULATION MODULE
160
TO CONTROLLER 165

FIG. 10

RATE ADAPTIVE CARDIAC RHYTHM MANAGEMENT DEVICE USING TRANSTHORACIC IMPEDANCE

This application is a divisional of application Ser. No. 09/032,731, filed Feb. 27, 1998, now U.S. Pat. No. 6,076,015

TECHNICAL FIELD OF THE INVENTION

This invention relates generally to cardiac rhythm management devices and methods and particularly, but not by way of limitation, to a rate adaptive cardiac rhythm management device using transthoracic impedance information, such as a minute ventilation signal, to control the rate at which pacing therapy is delivered to a patient's heart.

BACKGROUND OF THE INVENTION

Pacemakers and other cardiac rhythm management devices deliver cardiac therapy to a patient's heart to assist in obtaining a rhythm of heart contractions that maintains sufficient blood flow through the patient's circulatory system under a variety of conditions. In particular, rate-adaptive pacemakers deliver electrical pacing pulses to stimulate contractions of the heart. The rate at which the pulses are delivered is adjusted to accommodate a metabolic need of the patient. During exercise, higher pacing rates are delivered, while lower pacing rates are delivered when the patient is at rest.

Different parameters are used as an indication of the patient's metabolic need for pacing therapy, including: blood pH, blood temperature, electrocardiogram (ECG) artifacts such as QT interval, blood oxygen saturation, breathing rate, minute ventilation, etc. Pacemakers include specific control algorithms for tracking the parameter indicating metabolic need, and providing a control signal for adjusting the pacing rate accordingly. A variety of difficulties exist that complicate sensing of the parameter indicating metabolic need and controlling the pacing rate.

For example, detecting blood pH encounters sensor stability problems. pH sensors may drift with age and time. Blood oxygenation saturation is measured using light emitters that complicate the lead system used to couple the pacemaker's pulse generator to the heart. Blood temperature is a poor indicator of metabolic need because of the long time lag between the onset of exercise and any detectable increase in blood temperature. ECG artifacts, such as QT interval, are difficult to detect in the presence of other myopotentials and motion artifacts. Breathing rate, also referred to as respiratory rate, is not particularly well correlated with the need for increased blood circulation. For example, it is possible for respiratory rate to increase while the patient is sleeping or talking.

Minute ventilation (also referred to as "minute volume" or "MV") is a respiratory-related parameter that is a measure of the volume of air inhaled and exhaled during a particular period of time. Minute ventilation correlates well with the patient's metabolic need for an increased heart rate over a range of heart rates. A minute ventilation signal can be obtained by measuring transthoracic (across the chest or thorax) impedance. Transthoracic impedance provides respiratory or ventilation information, including how fast and how deeply a patient is breathing. A component of transthoracic impedance varies as the patient inhales and exhales. Ventilation (e.g., breathing rate, which is also referred to as "ventilation rate" or "VR", and breathing volume, which is also referred to as "tidal volume" or "TV") information is included in the impedance signal. A minute ventilation signal (also referred to as "minute volume" or "MV") signal is derived from the impedance signal, as illustrated by Equation 1. MV measures air flow rate (e.g., liters per minute), TV measures volume per breath (e.g., liters per breath), and VR measures breathing rate (e.g., breaths per minute).

$$MV=TV\times VR \quad (1)$$

A larger MV signal indicates a metabolic need for an increased heart rate, and the pacing rate can be adjusted accordingly by a cardiac rhythm management device. For example, one approach for measuring transthoracic impedance is described in Hauck et al., U.S. Pat. No. 5,318,597 entitled "RATE ADAPTIVE CARDIAC RHYTHM MANAGEMENT DEVICE CONTROL ALGORITHM USING TRANS-THORACIC VENTILATION," assigned to the assignee of the present application, the disclosure of which is incorporated herein by reference. However, many problems must be overcome to provide the most effective cardiac rhythm management therapy to the patient in a device that can remain implanted in the patient for a long period of time before requiring a costly surgical explantation and replacement procedure.

First, ventilation information included in the transthoracic impedance signal is confounded with a variety of extraneous signals that makes the ventilation information difficult to detect. For example, as the heart contracts during each cardiac cycle, its blood volume changes, contributing to a significant change in the transthoracic impedance signal that is unrelated to the ventilation information. The change in the transthoracic impedance signal due to blood volume changes resulting from heart contractions is referred to as cardiac "stroke volume" or "stroke" signal. Moreover, the frequencies of the heart contractions (e.g., 1–3 Hz) are extremely close to the frequency of the patient's breathing (e.g., under 1 Hz). This complicates separation of the stroke signal and the ventilation signal.

Furthermore, the frequency of the stroke and ventilation signals changes according to the patient's activity. For example, a resting patient may have a heart rate of 60 beats per minute and a ventilation rate of 10 breaths per minute. When exercising, the same patient may have a heart rate of 120 beats per minute and a ventilation rate of 60 breaths per minute. The changing frequencies of the stroke and ventilation signals further complicates the separation of these signals.

Another aspect of heart contractions also masks the ventilation signal. Heart contractions are initiated by electrical depolarizations (e.g., a QRS complex) resulting from paced or intrinsic heart activity. Such electrical heart activity signals may be detected during the measurement of transthoracic impedance. This further diminishes the accuracy of the transthoracic impedance measurement, and increases the difficulty of obtaining accurate ventilation information.

A further problem with certain other minute ventilation based cardiac rhythm management devices results from the use of a relatively high amplitude current pulse (e.g., 1 milliampere) to detect transthoracic impedance. Using high amplitude stimuli wastes power, risks capturing the heart (i.e., evoking a contraction), may trigger false detection of intrinsic heart activity by the pacemaker's sense amplifiers, and may produce a confusing or annoying artifact on electrocardiogram (ECG) traces or other diagnostic equipment.

Thus, there is a need for a cardiac rhythm management device that effectively manages the patient's heart rate based on an accurate indication of metabolic need. Such a cardiac

rhythm management device must be sufficiently robust to operate in the presence of extraneous noise signals that confound the indication of metabolic need. There is a further need for such a device to operate at low power consumption, in order to maximize the usable life of the battery-powered implantable device.

SUMMARY OF THE INVENTION

The present invention provides, among other things, a method of determining transthoracic impedance in a cardiac rhythm management device. A multiple phase stimulus is repeatedly delivered to a thorax region of a patient. More than one phase of each multiple phase stimuli is demodulated to obtain sample points of a response signal including transthoracic impedance information.

In one embodiment, a response to each phase is sampled, weighted to obtain a filtering function, and combined. In another embodiment, a rate of delivering cardiac rhythm management therapy is adjusted based on ventilation information included in the transthoracic impedance information of a plurality of the sample points. In another embodiment, a noise-response function inhibits rate-adjustment if the transthoracic impedance signal is too noisy. In a further embodiment, a interference avoidance function delays delivery of the multiple phase stimulus to avoid simultaneous occurrence with an interfering signal (e.g., a telemetry signal).

Another aspect of the invention includes a method of determining transthoracic impedance in a cardiac rhythm management device that includes delivering stimuli to a thorax of the patient, seasing a response signal including transthoracic impedance information, attenuating a component of the response signal having frequencies above a lowpass cutoff frequency, and adaptively basing the lowpass cutoff frequency on a heart rate, and independent of a breathing rate signal, from the patient.

In one such embodiment, a cardiac stroke signal is attenuated to obtain ventilation information. The lowpass cutoff frequency is adaptively selected to be below the heart rate by selecting between a number of discrete lowpass cutoff frequencies, each lowpass cutoff frequency corresponding to a particular range of values of the heart rate.

In a further embodiment, the method includes detecting peaks and valleys of the response signal. Differences between peaks and valleys of the response signal provide tidal volume data points, which are integrated for a predetermined period of time to obtain minute ventilation data points. A rate of delivering cardiac rhythm management therapy is adjusted based on the minute ventilation data points. Alternatively, breath-by-breath minute ventilation data points are obtained. Instead of performing the integration, time differences between the peaks and valleys of the response signal provide respiration period data points corresponding to the tidal volume data points. The tidal volume data points are divided by the corresponding respiration period data points to obtain minute ventilation data points, upon which a rate of delivering cardiac rhythm management therapy is adjusted.

Another aspect of the present invention includes a cardiac rhythm management device. The device includes an exciter, adapted to be coupled to a thorax of a patient for repeatedly delivering a multiphase stimulus thereto. A signal processor includes a receiver for obtaining transthoracic impedance information responsive to the stimuli. A demodulator, included in the signal processor, includes sampling elements for demodulating the transthoracic impedance in response to different phases of the multiphase stimulus. A therapy circuit is adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto. A controller is coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the transthoracic impedance.

In one embodiment, the device includes a noise-reversion circuit that inhibits rate-adjustment if the transthoracic impedance signal is too noisy. In a further embodiment, the device is included within a cardiac rhythm management system that also includes an endocardial lead, carrying first and second electrodes, and a housing including third and fourth electrodes.

Another aspect of the invention includes a cardiac rhythm management device that includes an exciter for delivering stimuli to a thorax. A signal processor includes a receiver for obtaining a transthoracic impedance responsive to the stimuli. The signal processor extracts ventilation information from the transthoracic impedance. The signal processor includes an adaptive lowpass filter for removing a cardiac stroke component of the transthoracic impedance signal. A cutoff frequency of the adaptive lowpass filter is adaptively based on a heart rate signal of the patient.

The cutoff frequency of the adaptive lowpass filter is independent of a breathing rate signal from the patient. A therapy circuit is adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto. A controller is coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the ventilation information.

The present invention provides, among other things, a cardiac rhythm management system, device, and methods that sense transthoracic impedance and adjust a delivery rate of the cardiac rhythm management therapy based on information extracted from the transthoracic impedance. The present invention effectively manages the patient's heart rate based on an accurate indication of metabolic need. It provides robust operation in the presence of extraneous noise signals that confound the indication of metabolic need. It also provides low power consumption, increasing the usable life of the battery-powered implantable device. Other advantages will be apparent upon reading the following detailed description of the invention, together with the accompanying drawings which form a part thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, like numerals describe substantially similar components throughout the several views.

FIG. **1** is a schematic/block diagram illustrating generally one embodiment of a cardiac rhythm management system according to the present invention, including a cardiac rhythm management device and electrode connections.

FIG. **2** is a schematic/block diagram illustrating generally one embodiment of particular circuits included within an exciter for delivering electrical excitation stimuli to a heart.

FIG. **3** illustrates generally a current waveform resulting from operation of an exciter according to one aspect of the present invention.

FIG. **4** is a block diagram illustrating generally one embodiment of portions of a signal processor.

FIG. **5** is a schematic diagram illustrating generally one embodiment of a preamplifier.

FIG. **6** is a schematic diagram illustrating generally one embodiment of a demodulator.

FIG. **7** is a signal flow diagram illustrating generally one embodiment of an adaptive filter.

FIG. **8** is a flow chart illustrating generally one example of a sequence of steps for calculating a minute ventilation indicated rate.

FIG. **9** is a flow chart illustrating generally a second example of a sequence of steps for calculating a minute ventilation indicated rate.

FIG. **10** is a block diagram illustrating generally an alternate embodiment of a signal processor.

DETAILED DESCRIPTION OF THE INVENTION

In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which is shown by way of illustration specific embodiments in which the invention may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention, and it is to be understood that the embodiments may be combined, or that other embodiments may be utilized and that structural, logical and electrical changes may be made without departing from the scope of the present invention. The following detailed description is, therefore, not to be taken in a limiting sense, and the scope of the present invention is defined by the appended claims and their equivalents.

Electrode Configuration and Top-Level Block Diagram

FIG. **1** is a schematic block diagram illustrating generally, by way of example, but not by way of limitation, one embodiment of a cardiac rhythm management system **100** according to the present invention. System **100** includes, among other things, cardiac rhythm management device **105** and leadwire ("lead") **110** for communicating signals between device **105** and a portion of a living organism, such as heart **115**. Embodiments of device **105** include bradycardia and antitachycardia pacemakers, cardioverters, defibrillators, combination pacemaker/defibrillators, drug delivery devices, and any other cardiac rhythm management apparatus capable of providing therapy to heart **115**. System **100** may also include additional components such as, for example, a remote programmer capable of communicating with device **105**.

In one embodiment, system **100** is implantable in the living organism, such as in a pectoral or abdominal region of a human patient, or elsewhere. In another embodiment, portions of system **100** (e.g., device **105**) are alternatively disposed externally to the human patient. In the illustrated embodiment, portions of lead **110** are disposed in the right ventricle, however, any other positioning of lead **110** is included within the present invention. For example, lead **110** may alternatively be positioned in the atrium or elsewhere. In one embodiment, lead **110** is a commercially available bipolar pacing lead. System **100** can also include other leads in addition to lead **110**, appropriately disposed, such as in or around heart **115**, or elsewhere.

In one embodiment, system **100** includes at least four electrodes, such as described in Hanck et al. U.S. Pat. No. 5,284,136 entitled "DUAL INDIFFERENT ELECTRODE PACEMAKER," assigned to the assignee of the present invention, the disclosure of which is incorporated herein by reference. It is understood, however, that the present invention also includes using a different number of electrodes (e.g., 2 or 3 electrodes, or more than 4 electrodes). In one example, a first conductor of multiconductor lead **110** electrically couples a first electrode, such as tip electrode **120** (e.g., disposed at the apex of the right ventricle of heart **115**), to device **105**. A second conductor of multiconductor lead **110** independently electrically couples a second electrode, such as ring electrode **125**, to device **105**. In one embodiment, device **105** includes a hermetically sealed housing **130**, formed from a conductive metal, such as titanium. Housing **130** (also referred to as a "case" or "can") is substantially covered over its entire surface by a suitable insulator, such as silicone rubber, except for at a window that forms a third electrode, referred to as a "case" or "can" electrode **135**. In one embodiment, a header **140** is mounted on housing **130** for receiving lead **110**. Header **140** is formed of an insulative material, such as molded plastic. Header **140** also includes at least one receptacle, such as for receiving lead **110** and electrically coupling conductors of lead **110** to device **105**. Header **140** also includes a fourth electrode, referred to as indifferent electrode **145**.

FIG. **1** also illustrates generally portions of device **105**, together with schematic illustrations of connections to the various electrodes. Device **105** includes an electrical stimulation source, such as exciter **150**. Exciter **150** delivers an electrical excitation signal, such as a strobed sequence of current pulses or other measurement stimuli, to heart **115** (e.g., between ring electrode **125** and tip electrode **120**, or using any other electrode configuration suitable for delivering the current pulses). In response to the excitation signal provided by exciter **150**, a response signal is sensed by signal processor **155** (e.g., between tip electrode **120** and indifferent electrode **145**, or any other suitable electrode configuration).

In one embodiment, the response signal sensed by signal processor **155** is a voltage that represents a transthoracic (i.e., across a portion of the chest or thorax) impedance. A minute ventilation signal (also referred to as "minute volume" or "MV") signal is derived from the impedance signal, as illustrated above by Equation 1. A larger MV signal indicates a metabolic need for an increased heart rate. According to one aspect of the invention, signal processor **155** extracts ventilation information, including the MV signal, from the impedance signal. Based on the MV signal, signal processor **155** outputs an indicated rate signal at node **160** to controller **165**. Based on the indicated rate signal at node **160**, controller **165** adjusts the rate of delivery of cardiac rhythm management therapy, such as electrical pacing stimuli, to heart **115** by therapy circuit **170**. Such pacing stimuli includes, for example, providing bipolar pacing between tip electrode **120** and ring electrode **125**, providing unipolar pacing between can electrode **135** and either of tip electrode **120** or ring electrode **125**, or providing pacing stimuli using any other suitable electrode configuration.

Exciter and Resulting Stimuli Waveform

FIG. **2** is a schematic/block diagram illustrating generally, by way of example, but not by way of limitation, one embodiment of particular circuits included within exciter **150** for delivering electrical stimuli (e.g., strobed alternating-direction constant-amplitude current pulses) to heart **115**. Exciter **150** includes, among other things, bridge switcher **200**, comprising switches **200A**, **200B**, **200C**, and **200D**. In one embodiment, switches **200A–D** are implemented as transistors, such as p-channel metal-oxide semiconductor (PMOS) field-effect transistors (FETs), or any other suitable switches.

Exciter **150** also includes current source **205** and current sink **210**. In one embodiment, each of current source **205** and current sink **210** include transistors in a regulated cascode or other suitable configuration. In one embodiment, switcher

200 is electrically coupled to case electrode 135 and ring electrode 125 through respective dc blocking capacitors 215A and 215B and respective switches 220A and 220B (e.g., PMOS transistors). Switches 225A and 225B (e.g., PMOS transistors) precharge respective capacitors 215A and 215B. Exciter 150 also includes a clock circuit 230 receiving one or more clock or other control signals from controller 165 and providing signals to the control terminals of each of switches 200A–D, 220A–B, and 225A–B.

FIG. 3 illustrates generally a current waveform 300 between case electrode 135 and ring electrode 125 resulting from operation of exciter 150 according to one aspect of the present invention. According to one aspect of the invention, waveform 300 includes a multiple phase ("multiphase") stimulus. In one embodiment, the multiphase stimulus includes a square wave, such as four current pulses 301, 302, 303, and 304 in sequentially alternating polarity/direction, each current pulse being a phase of the multiphase stimulus. In one embodiment, by way of example, but not by way of limitation, each one of current pulses 301–304 has a duration that is selected at approximately between 1 and 100 microseconds (e.g., approximately between 2 and 60 microseconds, such as at 20 microseconds), to allow adequate sampling of the transthoracic impedance signal obtained in response thereto. In the embodiment illustrated in FIG. 3, pulses 301–304 form a square wave having a carrier frequency of approximately 25 kilohertz. Other suitable durations of current pulses 301–304 could also be used, providing a different resulting carrier frequency. According to another aspect of the invention, the sequence of current pulses 301–304 is strobed. In one embodiment, by way of example, but not by way of limitation, the four pulse sequence 301–304 is repeated at a strobing frequency (also referred to as a repetition frequency or a sampling frequency) of approximately 20 Hertz (i.e., a 50 millisecond time interval). Other suitable strobing/repetition frequencies could also be used. For example, but not by way of limitation, any strobing repetition time interval shorter than 55 milliseconds could be used.

The amplitude of current pulses 301–304 was selected at less than approximately 1 milliampere. For example, approximately 320 microampere amplitude current pulses 301–304 provide an adequate excitation signal to obtain the desired response signal, while minimizing current drain of the implanted device 105, thereby increasing its implanted longevity. However, other amplitudes of current pulses 301–304 could also be used. Such amplitudes of current pulses 301–304 should be less than the tissue stimulation threshold of the heart to avoid any resulting cardiac depolarization. The strobing frequency is sufficiently fast to provide adequate sampling of ventilation or other information carried by the transthoracic impedance signal obtained in response to the electrical stimuli provided by exciter 150. Such ventilation information can appear at frequencies as high as approximately 1 Hertz, depending on the patient's breathing rate. The strobing frequency also minimizes aliasing of a "stroke volume" component of the transthoracic impedance signal (i.e., a portion of the transthoracic impedance signal that varies along with the patient's heartbeat instead of the patient's breathing rate). The stroke volume component of the transthoracic impedance signal can have frequencies as high as approximately 3 Hertz, depending on the patient's heart rate.

Prior to each sequence of current pulses 301–304, dc blocking capacitors 215A–B are precharged by a bias circuit, such as by turning on switches 200A–D and 225A–B, with switches 220A–B being off. Current source 205 and current sink 210 establish the operating point of a terminal of each of dc blocking capacitors 215A–B that is coupled to switcher 200. After precharging, switches 225A–B are turned off. Next, pulse 301 is produced by turning on switches 200A, 200D, and 220A–B, such that current delivered by current source 205 leaves case electrode 135. The current returns through ring electrode 125, and is sunk by current sink 210. Next, pulse 302 is produced by turning on switches 200B–C and 220A–B, such that current delivered by current source 205 leaves ring electrode 125. The current returns through case electrode 135, and is sunk by current sink 210. Next, pulse 303 is produced by again turning on switches 200A, 200D, and 220A–B, such that current delivered by current source 205 leaves case electrode 135. The current returns through ring electrode 125, and is sunk by current sink 210. Next, pulse 304 is produced by again turning on switches 200B–C and 220A–B, such that current delivered by current source 205 leaves ring electrode 125. The current returns through case electrode 135, and is sunk by current sink 210. Switches 220A–B, 200A–D, and 225A–B are turned off until precharging for another four current pulse sequence 301–304, which is delivered approximately 50 milliseconds later, as illustrated in FIG. 3.

According to one aspect of the invention, clock circuit 230 provides nonoverlapping control signals to switches 225A–B and switches 220A–B. As a result, switches 225A–B are not turned on at the same time as switches 220A–B. This avoids any coupling of either of case electrode 135 and ring electrode 125 to the positive power supply voltage V_{DD}.

Waveform 300 provides several important advantages allowing efficient and accurate sensing of the MV signal, allowing system 100 to provide more effective delivery of rate-responsive cardiac rhythm management therapy to the patient. First, system 100 allows the use of relatively low amplitude current pulses (e.g., +/–320 microamperes). This conserves power, allowing battery-powered portions of system 100 (e.g., device 105) to remain implanted in the patient for a longer usable lifetime. Because of their low amplitude, current pulses 301–304 do not produce any discernable artifacts on electrocardiogram (ECG) traces or on other diagnostic equipment. Such artifacts can confuse diagnosing physicians. The low amplitude current pulses 301–304 are also less likely to trigger false detection of intrinsic heart activity, such as by sense amplifiers included in device 105. False detection of intrinsic heart activity can inhibit proper delivery of pacing therapy, rendering cardiac rhythm management ineffective and increasing risk to the patient. According to one aspect of the present invention, the sensitivity setting of such sense amplifiers can be increased without being affected by interference from the current pulses 301–304 produced by exciter 150. Moreover, the low amplitude current pulses 301–304 avoid the risk of capturing heart 115 (i.e., inducing an electrical depolarization and heart contraction), particularly when current pulses 301–304 are delivered from small electrodes that are also used for delivering pacing therapy to heart 115.

According to another aspect of the invention, waveform 300 includes current pulses 301–304 that are strobed at a frequency of approximately 20 Hertz. The 25 kilohertz carrier frequency is only present for a short fraction of the 50 millisecond strobing time interval (i.e., duty cycle of less than 1%). The strobing also reduces power consumption and obtains increased implanted longevity of device 105, as described above.

Waveform 300 also provides balance in both amplitude and duration for each polarity/direction of the current pulses

301–304, thereby balancing the charge delivered to heart 115. Each +320 microampere pulse (e.g., 301 and 303) is balanced by an equal duration corresponding −320 microampere pulse (e.g., 302 and 304). This method of balancing the amplitude and duration of waveform 300 reduces the likelihood of capturing heart 115 or inducing false sensing as intrinsic heart activity sensed by device 105.

Interference Avoidance

In one embodiment, device 105 avoids delivering the multiphase stimulus in the presence of other interfering signals, such as telemetry signals, that increase the difficulty of accurately detecting a response. Referring again to FIG. 1, in one embodiment, device 105 includes a telemetry transceiver 185 for communicating via telemetry signals (e.g., telemetry pulses) with an external programmer 190, such as by inductively coupled coils in each of the device 105 and the external programmer 190. When telemetry pulses are detected by the telemetry receiver in device 105, and scheduled delivery of the multiphase stimulus coincides with the detection of the telemetry pulses, controller 165 delays delivery of the multiphase stimulus (e.g., current pulses 301–304), such as by approximately 1 millisecond. This avoids inaccuracies in the response signal to current pulses 301–304 that may result from the telemetry pulses or, similarly, from the presence of other interfering signals.

Signal Processor

FIG. 4 is a block diagram illustrating generally, by way of example, but not by way of limitation, one embodiment of portions of signal processor 155. Signal processor 155 includes analog signal processing circuit 400 and digital signal processing circuit 405. Inputs of a preamplifier 410 (also referred to as a preamp or a receiver) of analog signal processing circuit 400 are electrically coupled to each of indifferent electrode 145 and tip electrode 120 for receiving a signal in response to the above-described stimuli provided by exciter 150. Analog signal processing circuit 400 also includes demodulator 415, receiving the output of preamplifier 410, and providing an output signal to bandpass filter 420. An output signal from bandpass filter 420 is received by analog-to-digital (A/D) converter 425. An output signal from A/D converter 425 is received at highpass filter 430 of digital signal processing circuit 405.

In one embodiment, digital signal processing circuit 405 is included within controller 165 such as, for example, as a sequence of instructions executed by a microprocessor. In another embodiment, digital signal processing circuit 405 includes separately implemented hardware portions dedicated to performing the digital signal processing tasks described below. An output signal from highpass filter 430 is received by adaptive lowpass filter 435 of digital signal processing circuit 405. Minute ventilation calculation module 440 receives an output signal from adaptive lowpass filter 435, and provides a resulting indicated rate signal at node 160 to controller 165.

Preamplifier

FIG. 5 is a schematic diagram illustrating generally, by way of example, but not by way of limitation, one embodiment of preamplifier 410. Preamplifier 410 includes a switched-capacitor (SC) differential amplifier 500. Preamplifier 410 is electrically coupled to indifferent electrode 145 and tip electrode 120 through respective switches 510 and 515 and respective resistors 520 and 525. Switches 510 and 515 are turned on only during the approximate time when the stimuli current pulses 301–304 are being delivered by exciter 150. Resistors 520 and 525 provide antialiasing/bandlimiting of the input signals received from indifferent electrode 145 and tip electrode 120.

Differential amplifier 500 includes input capacitors 530 and 535, coupled to resistors 520 and 525 respectively, and also coupled to a respective positive input at node 540 and a negative input, at node 545, of a differential-input/differential-output operational amplifier 550. Feedback capacitors 560 and 565 are coupled from a respective negative output, at node 570, and a positive output, at node 575, of operational amplifier 550, to its respective positive input, at node 540, and negative input, at node 545. In one embodiment, input capacitors 530 and 535 have approximately 10 times the capacitance value of respective feedback capacitors 560 and 565.

Differential amplifier 500 also includes autozeroing input switches, 580 and 585, coupling respective input nodes 540 and 545 to respective reference voltages (e.g., a ground voltage). Autozeroing output switches 590 and 595 couple respective output nodes 570 and 575 to respective reference voltages (e.g., a ground voltage). Switches 580, 585, 590, and 595 provide zeroing of corresponding feedback capacitors 560 and 565. Switches 580 and 585 further establish the bias points of the input nodes 540 and 545 of operational amplifier 550, such as during sampling of signals from indifferent electrode 145 and tip electrode 120 onto input capacitors 530 and 535.

Preamplifier 410 receives a voltage based on the transthoracic impedance between indifferent electrode 145 and tip electrode 120. For example, a transthoracic impedance of 50 ohms results in a voltage between the inputs of differential amplifier 500 of approximately 16 millivolts. The transthoracic impedance varies as the patient breathes, increasing as air fills the patient's thoracic cavity during inspiration and decreasing as air is released during expiration. The transthoracic impedance may vary, for example, by approximately 2 ohms during respiration, resulting in an approximately 0.64 millivolt modulation of the approximately 16 millivolt baseline signal appearing between the inputs of differential amplifier 500. These impedance and voltage values are recited by way of example only; actual impedance and voltage values will vary according to, among other things, differences in patient anatomy and electrode placement.

In one embodiment of the invention, by way of example, but not by way of limitation, the electrodes used for delivering the excitation current (e.g., ring electrode 125 and case electrode 135) are different from the electrodes used for sensing the response thereto (e.g., indifferent electrode 145 and tip electrode 120). This advantageously reduces the magnitude of the baseline component of the transthoracic impedance signal, thereby increasing the relative contribution of the ventilation component of the transthoracic impedance signal, and increasing the signal-to-noise ratio (SNR). Alternatively, the same electrodes could be used for delivering the excitation current and sensing the response thereto.

In one embodiment, differential amplifier 500 provides an effective voltage gain of approximately 6. In the above example, the 16 millivolt baseline signal is amplified to approximately 100 millivolts by differential amplifier 500 and the resulting signal is provided to demodulator 415.

Demodulator

Demodulator 415 samples the signal obtained in response to current pulses 301–304 after the above-described amplification by preamplifier 410. According to one aspect of the

invention, the output of preamplifier **410** is sampled at the end of each of current pulses **301**–**304**. Demodulator **415** combines these four samples into a single value using a weighted average. The resulting weighted average represents the total impedance (i.e., including both baseline and ventilation components) obtained for the sequence of four current pulses **301**–**304**.

In one embodiment, the weighted average is formed by weighting the second and third samples, obtained from respective current pulses **302** and **303**, by a factor of approximately 3.0 relative to the first and fourth samples, obtained from respective current pulses **301** and **304**. Weighting the samples advantageously provides an additional highpass filtering function, substantially transmitting the transthoracic impedance signal at the 25 kilohertz carrier frequency of the current pulses **301**–**304**, while substantially rejecting out-of-band signals. In particular, demodulator **415** provides additional rejection of low-frequency signals, such as R-waves and other electrical signals produced by heart **115**. A transfer function provided by one embodiment of demodulator **415**, is described in the z-domain, as illustrated in Equation 2.

$$H(z)=0.2(0z^{-1}-3z^{-2}+3z^{-3}-1z^{-4}) \quad (2)$$

In this embodiment, demodulator **415** provides a voltage gain that is approximately between 1.75 and 2.0 for the in-band transthoracic impedance signal. Moreover, demodulator **415** also advantageously attenuates signals at frequencies below 100 Hz by a factor of at least approximately 120 dB, including such signals as R-waves and other electrical intrinsic heart activity signals produced by heart **115**, which can interfere with sensing the patient's transthoracic impedance.

FIG. **6** is a schematic diagram illustrating generally, by way of example, but not by way of limitation, one embodiment of a switched-capacitor demodulator **415**. The output signal from preamplifier **410** is sampled onto capacitors **600**A–B in response to current pulse **301**, onto capacitors **605**A–B in response to current pulse **302**, onto capacitors **610**A–B in response to current pulse **303**, and onto capacitors **615**A–B in response to current pulse **304**. Capacitors **605**A–B and **610**A–B provide 3 times the capacitance value of capacitors **600**A–B and **615**A–B, in order to provide the above-described weighting of the samples. After the weighted sampling of the output of preamplifier **410** in response to the four current pulses **301**–**304**, these weighted samples are summed by switched-capacitor integrator **620** (also referred to as a summer).

Also illustrated in FIG. **6** are dummy capacitors **625**A–B. Each of dummy capacitors **625**A–B has a capacitance value that is twice that of one of capacitors **600**A–B, and twice that of one of capacitors **615**A–B. Dummy capacitors **625**A–B are switched in during sample of current pulses **301** and **304**. As a result, demodulator **415** presents the same load capacitance to preamplifier **410** during sampling of each of the four current pulses **301**–**304**. As seen in FIG. **6**, however, the charge that is sampled onto dummy capacitors **625**A–B is not included in the weighted sample (i.e., the resulting charge is not included in the integration provided by integrator **620**). Furthermore, it is understood that, in one embodiment, the capacitors illustrated in FIG. **6** are initialized (e.g., discharged) prior to sampling any particular sequence of current pulses **301**–**304**.

In FIG. **6**, integrator **620** includes input capacitors **650** and **655**, which are autozeroed by switches, as illustrated, during the clock phase $\phi_{1/}$. An integration capacitor **660**, which is in the feedback path around operational amplifier **665**, sums the weighted samples obtained in response to the four current pulses **301**–**304** during an integration clock phase ϕ_I. A noise sampling/integration capacitor **630**, which is also in the feedback path around operational amplifier **665**, sums the weighted samples obtained in the absence of delivered current pulses during a noise integration clock phase ϕ_{NI}, as described below. Integrator **620** also provides a matching network **670** on the other input of operational amplifier **665** for matching the above-described switched capacitor operation.

In one embodiment, demodulator **415** also provides a noise sensing mode of operation. In normal operation, demodulator **415** samples the output of filter/amplifier **410** in response to current pulses **301**–**304** provided by exciter **150**. During a noise sensing mode of operation, exciter **150** is turned off (i.e., current pulses **301**–**304** are not provided), and demodulator **415** samples, onto switched-in noise sampling/integration capacitor **630**, noise arising from external sources (e.g., heart signals or any environmental noise sources) and internal noise produced by circuits coupled to the input of the demodulator **415**. In particular, demodulator **415** is capable of sensing noise that is at frequencies close to the 25 kilohertz carrier frequency of the current pulses **301**–**304**.

In one embodiment, the gain of demodulator **415** is increased (e.g., by a factor of approximately 2.0–2.5) during noise sensing mode in order to provide more sensitive noise detection. For example, the noise sampling/integration capacitor **630** used during noise sensing is different in value from a corresponding integration capacitor used during normal operation of demodulator **415**, in order to provide a different gain during noise sensing.

According to one aspect of the invention, device **105** also includes a noise reversion circuit based on the noise sensed by demodulator **415** when exciter **150** is turned off. A noise comparator **635** receives a signal derived from the output of demodulator **415**. Comparator **635** determines whether the detected noise exceeds a particular programmable threshold value. If the detected noise exceeds the threshold value, subsequent circuits ignore the output of demodulator **415** (e.g., until the detected noise again falls below the threshold value). In one embodiment, the programmable threshold value used by comparator **635** is implemented as a programmable switched-capacitor array, providing threshold voltages ranging between approximately 4–120 millivolts at the output of demodulator **415** (corresponding to an impedance noise threshold between approximately 0.4–12 ohms).

Bandpass Filter

In one embodiment, bandpass filter **420** provides a passband between single pole corner frequencies at 0.1 Hz and 2.0 Hz, and includes a gain stage providing a voltage gain that is programmable (e.g., 6x, 12x, and 24x). The 0.1 Hz low frequency (highpass) pole substantially attenuates the baseline component of the transthoracic impedance signal, but substantially transmits the time-varying component of the transthoracic impedance signal representing ventilation. The 2.0 Hz high frequency (lowpass) pole substantially attenuates other time-varying components of the transthoracic impedance signal that do not contribute substantial ventilation information. In particular, the lowpass pole effectively contributes to the attenuation of signal components due to the cardiac stroke signal resulting from the beating of heart **115**. As described above, removal of the stroke signal is both difficult and particularly important for properly adapting the delivered pacing rate based on minute ventilation, since the stroke signal is very close in frequency

to the desired ventilation signal. The lowpass pole also filters out other noise at frequencies that exceed the lowpass pole frequency.

Many different implementations of bandpass filter **420** will be suitable for use in the present invention. In one embodiment, bandpass filter **420** includes a switched-capacitor biquadratic filter stage, series-coupled with a subsequent switched-capacitor gain stage. Capacitance values of the switched-capacitor gain stage are user-programmable, thereby obtaining differing voltage gains, as described above. The output of the switched capacitor gain stage included in bandpass filter **420** is provided to the input of A/D converter **425**.

Analog-to-Digital (A/D) Converter

A/D converter **425** receives the output signal of bandpass filter **420** and provides a resulting digitized output signal to highpass filter **430** of digital signal processing circuit **405**. In one embodiment, A/D converter **425** is implemented as an 8-bit, successive approximation type switched-capacitor A/D converter having an input range of approximately 1 Volt. According to one aspect of the invention, A/D converter **425** provides one 8-bit digital word corresponding to each sequence of four current pulses **301**–**304** delivered by exciter **150**. Many different implementations of A/D converter **425** will be suitable for use in the present invention. For example, a different A/D converter resolution (greater than or less than 8 bits) may be used.

Digital Signal Processing Circuit

Highpass filter **430** includes, in one embodiment, a single-pole infinite impulse response (IIR) digital filter that receives the 8-bit digital output signal from A/D converter **425**, removing frequency components below its highpass cutoff frequency of approximately 0.1 Hz. Many other different embodiments of highpass filter **430** will also be suitable for use in the present invention. Highpass filter **430** advantageously further attenuates baseline dc components of the transthoracic impedance and any dc offset voltages created by A/D converter **425**. The output of highpass filter **430** is provided to adaptive lowpass filter **435**.

Adaptive lowpass filter **435** receives the output signal of highpass filter **430** and attenuates frequency components of the signal that exceed the lowpass cutoff frequency of adaptive lowpass filter **435**. Attenuated frequencies include the cardiac stroke signal, resulting from changes in blood volume in heart **115** as it contracts during each cardiac cycle, which appears as a component of the transthoracic impedance signal. Thus, the cardiac stroke signal confounds the desired ventilation information indicating the metabolic need for adjusting pacing rate.

As described above, the component of the transthoracic impedance due to the stroke signal can be substantial. As a result, attenuation of the stroke signal is particularly important for properly adapting the delivered pacing rate based on minute ventilation. Moreover, the stroke signal is difficult to attenuate, since it is very close in frequency to the desired ventilation signal. Furthermore, the frequencies of each of the stroke and ventilation signals varies according to the patient's activity, making the stroke and ventilation signals difficult to separate.

Adaptive lowpass filter **435** provides effective attenuation of the stroke component of the processed transthoracic impedance signal received from highpass filter **430**. Frequency components above a lowpass cutoff frequency are attenuated. In one embodiment, the frequency components above the lowpass cutoff frequency are attenuated by at least 30 decibels while preserving ventilation information having frequency components below the lowpass cutoff frequency. The lowpass cutoff frequency is adaptively based on a heart rate of the patient and, according to a further aspect of the invention, is independent of any breathing rate signal obtained from the patient. In one embodiment, the patient's heart rate is detected by sense amplifiers **175**, and provided to adaptive lowpass filter **435**, such as by controller **165**, for adjusting the lowpass cutoff frequency of adaptive lowpass filter **435** accordingly. Table 1 illustrates, by way of example, but not by way of limitation, one mapping of different lowpass cutoff frequencies of adaptive lowpass filter **435** to ranges of the patient's heart rate. Other mappings may also be used.

TABLE 1

Exemplary lowpass cutoff frequencies of adaptive lowpass filter 435 based on different sensed heart rates.

Heart Rate (beats per minute)	Lowpass cutoff frequency
<68	0.5 Hz
68–88	0.75 Hz
>88	1.0 Hz

As Table 1 illustrates, a 0.5 Hz cutoff frequency is used when the sensed heart rate is less than 68 beats per minute. When the patient's heart rate increases above 68 beats per minute, adaptive lowpass filter **435** switches its lowpass cutoff frequency to 0.75 Hz. When the patient's heart rate increases above 88 beats per minute, adaptive lowpass filter **435** switches its lowpass cutoff frequency to 1.0 Hz. Similarly, as heart rate decreases, adaptive lowpass filter **435** adjusts the lowpass cutoff frequency according to Table 1. As a result, adaptive lowpass filter **435** preserves the ventilation information at higher breathing rates (breathing rate increases together with heart rate), while continuing to attenuate the stroke signal.

The present invention bases adaptive adjustment of the lowpass cutoff frequency only on heart rate. Among other things, this reduces computational complexity and power consumption associated with monitoring the breathing rate for adjusting the lowpass cutoff frequency. This also ensures that adaptive lowpass filter **435** removes the stroke signal for all particular combinations of respiration rate and heart rate, so that pacing rate is appropriately adjusted based on minute ventilation.

In one embodiment, adaptive filter **435** uses a 4-pole Chebyshev filter that is better suited to data represented by fewer bits (e.g., 8-bit fixed point arithmetic). This conserves power and avoids instability and other potential problems of quantization. According to one aspect of the invention, adaptive lowpass filter **435** uses a state-space structure, rather than in a conventional direct form structure. The state-space structure further reduces the effects of coefficient quantization and roundoff noise. One example of such a state-space structure is described in Leland B. Jackson, "Digital Filters and Signal Processing," 2nd ed., pp. 332–340, Kluwer Academic Publishers, Boston, Mass., the disclosure of which is incorporated herein by reference.

FIG. **7** is a signal flow diagram illustrating generally one embodiment of adaptive filter **435** having a state-space topology. FIG. **7** includes scaling elements, delay elements, and summation elements. Signals output from summation elements are also scaled, as illustrated in FIG. **7**. As with any DSP filter, saturation of signals at particular nodes should be

avoided by adjusting the coefficients according to conventional DSP coefficient scaling techniques. One embodiment of hexadecimal values of filter coefficients is illustrated by way of example, but not by way of limitation, in Table 2.

Adaptive lowpass filter **435** outputs a signal based on transthoracic impedance and carrying ventilation information. The stroke component of the transthoracic impedance signal is substantially removed. The output of adaptive lowpass filter **435** is provided to MV calculation module **440**, which calculates a minute ventilation indicated pacing rate based on the ventilation information.

TABLE 2

Exemplary Scaling Coefficients for Adaptive Filter 435

Scaling Element (Hexadecimal)	Coefficient for 0.5 Hz Lowpass Cutoff Frequency (Hexadecimal)	Coefficient for 0.75 Hz Lowpass Cutoff Frequency (Hexadecimal)	Coefficient for 1.0 Hz Lowpass Cutoff Frequency (Hexadecimal)
1B1	40	22	28
1B2	00	00	00
1A11	77	75	72
1A12	FF	C6	9B
1A21	92	88	85
1A22	8C	8B	89
1C1	01	FF	FF
1C2	40	60	7A
1D	04	18	15
2B1	20	10	0F
2B2	00	01	01
2A11	3F	33	2F
2A12	C8	FD	FD
2A21	01	0C	18
2A22	8F	33	2F
2C1	03	02	06
2C2	49	3A	3D
2D	10	05	07

Minute Ventilation Calculation Module

In one embodiment, MV calculation module **440** is implemented as a sequence of instructions executed on any suitable microprocessor, such as a Zilog **280**-type microprocessor. Alternatively, MV calculation module **440** is implemented as any other hardware or software configuration capable of calculating an indicated pacing rate based on ventilation information. One example of such a sequence of instructions executed on a microprocessor for calculating a minute ventilation indicated rate is described below, and illustrated in the flow chart of FIG. **8**.

MV calculation module **440** receives from adaptive lowpass filter **435** a digital signal representing a time-varying transthoracic impedance. In one embodiment, the impedance signal is centered around zero, with positive values representing inhalation, and negative values representing exhalation. At step **800**, the maximum (most positive) and minimum (most negative) values of the impedance signal are stored in separate storage registers. After each breath, an interrupt is provided to the microprocessor, such as upon each positive-going zero-crossing.

At step **805**, the tidal volume (TV) is calculated upon receiving the interrupt. The tidal volume is obtained by reading the storage registers, and taking the difference between the maximum and minimum values of the impedance signal held for the patient's previous breath. A larger tidal volume indicates a deeper breath than a smaller tidal volume. A tidal volume data point is produced at step **805** for each breath by the patient.

At step **810**, the tidal volume is integrated (i.e., the tidal volume data points are summed) for a predetermined period of time (e.g., approximately 8 seconds), obtaining a minute ventilation data point, as described in Equation 1. After each 8 second integration period, the minute ventilation data point is output, and a new integration (i.e., summation) of tidal volume commences.

Steps **815** and **820**, include carrying out concurrent moving short term and long term averages, respectively. More particularly, the short term average ("STA," also referred to as a "boxcar" average) at step **815** represents, at a particular point in time, a moving average of the minute ventilation data points over the previous approximately 32 seconds. The short term average represents the present minute ventilation indication of metabolic need. Similarly, the long term average ("LTA") at step **820** represents, at a particular point in time, a moving average of the minute ventilation data points over the previous approximately 2 hours. The long term average approximates the resting state of the minute ventilation indicator. In one embodiment, the long term average at step **820** is carried out by an IIR digital filter.

At step **825**, the short term and long term averages are compared. In one embodiment, this comparison involves subtracting the long term average from the short term average. The difference is optionally scaled, and used to adjust the pacing rate when the short term average exceeds the long term average. In one embodiment, the rate is adjusted according to Equation 3.

$$RATE_{MV}=LRL+K(STA-LTA) \tag{3}$$

In Equation 3, STA represents the short term average, LTA represents the long term average, K represents an optional scaling coefficient, LRL is a programmable lower rate limit to which the incremental sensor driven rate is added, and $RATE_{MV}$ is the minute ventilation indicated rate at which pacing therapy is delivered. In this embodiment, $RATE_{MV}$ is a linear function of the difference STA–LTA. Also, in this embodiment, if the value of the short term average is less than the value of the long term average, pacing therapy is delivered at the lower rate limit (LRL).

In one embodiment of the invention, more than one scaling coefficient K is used, obtaining a piecewise linear mapping of minute ventilation to the resulting minute ventilation indicated rate. For example, when the STA–LTA difference exceeds a certain threshold value, a smaller scaling coefficient K is used. This reduces the incremental increase in pacing rate for high pacing rates, when compared to the incremental increase in pacing rate for pacing rates close to the lower rate limit (LRL).

Step **825** is alternatively implemented as a ratio STA/LTA, rather than the difference STA–LTA. In one such embodiment, the rate is adjusted according to Equation 4 when STA exceeds LTA.

$$RATE_{MV}=LRL+C\left(\frac{STA}{LTA}\right) \tag{4}$$

In Equation 4, STA represents the short term average, LTA represents the long term average, C represents an optional scaling coefficient, LRL is a programmable lower rate limit to which the incremental sensor driven rate is added, and $RATE_{MV}$ is the minute ventilation indicated rate at which pacing therapy is delivered. If the value of the short term average is less than the value of the long term average, pacing therapy is delivered at the lower rate limit (LRL). In this embodiment, reduced incremental rate at high pacing rates is obtained by using more than one scaling coefficient, as described above.

Other rate modifiers can also be used to obtain a minute ventilation indicated rate. Moreover, the minute ventilation indicated rate can be combined, blended, or otherwise used in conjunction with other rate indicators, such as those derived from different sensors providing different indicators of metabolic need (e.g., acceleration). Such indicators may have different response characteristics (e.g., time lag after onset of exercise) that are advantageously combined with the minute ventilation rate indication described above.

At step **830**, the indicated rate (e.g., $RATE_{ADJ}$) is provided to controller **165**, for adjusting the rate of pacing therapy delivered by therapy circuit **170**.

Minute Ventilation Calculation Alternate Embodiment

FIG. **9** is a flow chart, similar to that of FIG. **8**, illustrating generally another embodiment of the invention that uses a breath-by-breath minute ventilation calculation. At step **900**, time differences corresponding to the peaks and valleys of the response signal are used to obtain respiration period data points corresponding to the tidal volume data points obtained in step **805**. At step **910**, a breath-by-breath indication of minute ventilation is obtained, such as by dividing the tidal volume data points by the corresponding respiration period data points to obtain minute ventilation data points. The rate of delivering cardiac rhythm management therapy is then adjusted based on the minute ventilation data points, as described above with respect to FIG. **8**.

Signal Processor Alternate Embodiment

The above description illustrates, by way of example, but not by way of limitation, a particular embodiment of the signal processor **155**, as illustrated in FIG. **4**, and methods for its use. Many other possible embodiments of signal processor **155** exist and are also included within the present invention. FIG. **10** is a block diagram illustrating generally one such variation on signal processor **155**. The bandpass filter **420** of FIG. **4** is implemented digitally in the signal processor **155** of FIG. **10**. Other variations are also possible without departing from the present invention.

Rate Adjustment Alternate Embodiment

The above description illustrates, by way of example, but not by way of limitation, a particular embodiment of the present invention in which ventilation information is extracted from a detected transthoracic impedance, and the rate of delivery of cardiac rhythm management therapy is adjusted based on an indicator derived from the ventilation information. However, the present invention also includes the extraction of other information (e.g., cardiac stroke information) from the transthoracic impedance, such as for adjusting the rate of delivery of cardiac rhythm management therapy based on an indicator extracted from such information. One such example is disclosed in Warren et al. U.S. Pat. No. 5,156,147 entitled, "VARIABLE RATE PACEMAKER HAVING UPPER RATE LIMIT GOVERNOR BASED ON HEMODYNAMIC PERFORMANCE," which is assigned to the assignee of the present invention, and the disclosure of which is incorporated herein by reference. Another such example is disclosed in Spinelli U.S. Pat. No. 5,235,976 entitled, "METHOD AND APPARATUS FOR MANAGING AND MONITORING CARDIAC RHYTHM MANAGEMENT USING ACTIVE TIME AS THE CONTROLLING PARAMETER," which is assigned to the assignee of the present invention, and the disclosure of which is incorporated herein by reference.

Conclusion

The present invention provides, among other things, a cardiac rhythm management device that senses transthoracic impedance and adjusts a delivery rate of the cardiac rhythm management therapy based on information extracted from the transthoracic impedance. In one embodiment, an adaptive lowpass filter removes the stroke signal from the transthoracic impedance signal while preserving the ventilation information. The adaptive filter includes a lowpass cutoff frequency that is adaptively based on the patient's heart rate, but independent of a breathing rate signal. A weighted demodulation provides filtering that enhances rejection of unwanted signals. Minute ventilation is obtained from tidal volume obtained from the ventilation information. An indicated rate is based on a difference between, or ratio of, short and long term averages of the minute ventilation information, unless noise exceeding a threshold is detected.

The present invention effectively manages the patient's heart rate based on an accurate indication of metabolic need. It provides robust operation in the presence of extraneous noise signals that confound the indication of metabolic need. It also provides low power consumption, increasing the usable life of the battery-powered implantable device.

It is to be understood that the above description is intended to be illustrative, and not restrictive. Many other embodiments will be apparent to those of skill in the art upon reviewing the above description. The scope of the invention should, therefore, be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled.

What is claimed is:

1. A cardiac rhythm management device, comprising:

an exciter, adapted to be coupled to a thorax of a patient for repeatedly delivering a multiphase stimulus thereto;

a signal processor, including a receiver for obtaining transthoracic impedance information responsive to the stimuli;

a demodulator, included in the signal processor, the demodulator including sampling elements for demodulating the transthoracic impedance in response to different phases of the multiphase stimulus, where the demodulator combines weighted samples of the transthoracic impedance information to attenuate unwanted signals;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the transthoracic impedance.

2. The device of claim **1**, in which the exciter includes a bridge switcher providing the multiphase stimulus.

3. The device of claim **2**, in which the exciter includes:

first and second capacitors, adapted for coupling the bridge switcher to the thorax of the patient; and

a bias circuit for precharging the first and second capacitors.

4. The device of claim **1**, in which the demodulator includes a switched-capacitor sampler and integrator.

5. The device of claim **4**, in which the switched capacitor sampler includes capacitors that weight pulses corresponding to the phases in the multiphase stimulus.

6. The device of claim **1**, further comprising:

a noise-reversion circuit coupled to the demodulator for receiving a noise response signal in the absence of stimuli;

a noise comparator, included in the noise-reversion circuit, for comparing the noise response signal to a threshold value, and providing a resulting noise comparator output signal indicating whether the noise response signal exceeds the threshold value; and

wherein the controller adjusts the rate of delivery of the cardiac rhythm management therapy independent of the transthoracic impedance if the comparator output indicates that the noise response signal exceeds the threshold value.

7. A cardiac rhythm management system, including the cardiac rhythm management device of claim **1**, the cardiac rhythm management system further comprising:

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

8. The cardiac rhythm management system of claim **7**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

9. The cardiac rhythm management system of claim **8**, wherein the indifferent electrode is carried by a header portion of the housing.

10. A cardiac rhythm management device comprising:

an exciter, adapted to be coupled to a thorax of a patient for delivering stimuli thereto;

a signal processor, including a receiver for obtaining a transthoracic impedance responsive to the stimuli, the signal processor extracting ventilation information from the transthoracic impedance, wherein the signal processor includes an adaptive lowpass filter for removing a cardiac stroke component of the transthoracic impedance signal, a cutoff frequency of the adaptive lowpass filter being adaptively based on a heart rate of the patient, the cutoff frequency of the adaptive lowpass filter being independent of a breathing rate signal from the patient;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the ventilation information.

11. The device of claim **10**, in which the signal processor includes:

an analog signal processing circuit, receiving the transthoracic impedance signal and including an analog-to-digital (A/D) converter providing a responsive digital transthoracic impedance signal; and

wherein the adaptive lowpass filter includes a digital 4-pole Chebyshev filter including a state-space structure.

12. The device of claim **10**, wherein the controller selects the cutoff frequency of the adaptive lowpass filter to be higher when the heart activity signal indicates a higher heart rate and lower when the heart activity signal indicates a lower heart rate.

13. The device of claim **10**, wherein the controller selects between a number of discrete lowpass cutoff frequencies, each lowpass cutoff frequency corresponding to a particular range of values of the heart rate

14. The device of claim **13**, wherein the controller selects the cutoff frequency of the adaptive lowpass filter at approximately 0.5 Hz, 0.75 Hz, and 1.0 Hz when the heart rate is respectively approximately less than 68 beats per minute, between 68 and 88 beats per minute, and greater than 88 beats per minute.

15. A cardiac rhythm management system, including the cardiac rhythm management device of claim **10**, the cardiac rhythm management system further comprising:

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

16. The cardiac rhythm management system of claim **15**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

17. The cardiac rhythm management system of claim **16**, wherein the indifferent electrode is carried by a header portion of the housing.

18. A cardiac rhythm management device, comprising:

an exciter, adapted to be coupled to a thorax of a patient for repeatedly delivering a multiphase stimulus thereto;

a signal processor, including a receiver for obtaining transthoracic impedance information responsive to the stimuli;

a demodulator, included in the signal processor, the demodulator including sampling elements for demodulating the transthoracic impedance in response to different phases of the multiphase stimulus and a switched-capacitor sampler and integrator, where the switched capacitor sampler includes capacitors that weight pulses corresponding to the phases in the multiphase stimulus;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the transthoracic impedance.

19. The device of claim **18**, in which the exciter includes a bridge switcher providing the multiphase stimulus.

20. The device of claim **19**, in which the exciter includes:

first and second capacitors, adapted for coupling the bridge switcher to the thorax of the patient; and

a bias circuit for precharging the first and second capacitors.

21. The device of claim **18**, further comprising:

a noise-reversion circuit coupled to the demodulator for receiving a noise response signal in the absence of stimuli;

a noise comparator, included in the noise-reversion circuit, for comparing the noise response signal to a threshold value, and providing a resulting noise comparator output signal indicating whether the noise response signal exceeds the threshold value; and

wherein the controller adjusts the rate of delivery of the cardiac rhythm management therapy independent of the transthoracic impedance if the comparator output indicates that the noise response signal exceeds the threshold value.

22. A cardiac rhythm management system, including the cardiac rhythm management device of claim **18**, the cardiac rhythm management system further comprising:

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

23. The cardiac rhythm management system of claim **22**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

24. The cardiac rhythm management system of claim **23**, wherein the indifferent electrode is carried by a header portion of the housing.

25. A cardiac rhythm management device, comprising:

an exciter, adapted to be coupled to a thorax of a patient for repeatedly delivering a multiphase stimulus thereto;

a signal processor, including a receiver for obtaining transthoracic impedance information responsive to the stimuli;

a demodulator, included in the signal processor, the demodulator including sampling elements for demodulating the transthoracic impedance in response to different phases of the multiphase stimulus;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto;

a noise-reversion circuit coupled to the demodulator for receiving a noise response signal in the absence of stimuli;

a noise comparator, included in the noise-reversion circuit, for comparing the noise response signal to a threshold value, and providing a resulting noise comparator output signal indicating whether the noise response signal exceeds the threshold value; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the transthoracic impedance, wherein the controller adjusts the rate of delivery of the cardiac rhythm management therapy independent of the transthoracic impedance if the comparator output indicates that the noise response signal exceeds the threshold value.

26. The device of claim **25**, in which the exciter includes a bridge switcher providing the multiphase stimulus.

27. The device of claim **26**, in which the exciter includes:

first and second capacitors, adapted for coupling the bridge switcher to the thorax of the patient; and

a bias circuit for precharging the first and second capacitors.

28. The device of claim **25**, in which the demodulator includes a switched-capacitor sampler and integrator.

29. The device of claim **28**, in which the switched capacitor sampler includes capacitors that weight pulses corresponding to the phases in the multiphase stimulus.

30. A cardiac rhythm management system, including the cardiac rhythm management device of claim **25**, the cardiac rhythm management system further comprising:

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

31. The cardiac rhythm management system of claim **30**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

32. The cardiac rhythm management system of claim **31**, wherein the indifferent electrode is carried by a header portion of the housing.

33. A cardiac rhythm management device comprising:

an exciter, adapted to be coupled to a thorax of a patient for repeatedly delivering a multiphase stimulus thereto;

a signal processor, including a receiver for obtaining transthoracic impedance information responsive to the stimuli;

a demodulator, included in the signal processor, the demodulator including sampling elements for demodulating the transthoracic impedance in response to different phases of the multiphase stimulus;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto;

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the transthoracic impedance;

an endocardial lead, carrying first and second electrodes adapted to be implanted in the heart, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

34. The cardiac rhythm management system of claim **33**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

35. The cardiac rhythm management system of claim **34**, wherein the indifferent electrode is carried by a header portion of the housing.

36. A cardiac rhythm management device comprising:

an exciter, adapted to be coupled to a thorax of a patient for delivering stimuli thereto;

a signal processor, including a receiver for obtaining a transthoracic impedance responsive to the stimuli, the signal processor extracting ventilation information from the transthoracic impedance, wherein the signal processor includes an adaptive lowpass filter for removing a cardiac stroke component of the transthoracic impedance signal, a cutoff frequency of the adaptive lowpass filter being adaptively based on a heart rate of the patient, the cutoff frequency of the adaptive lowpass filter being independent of a breathing rate signal from the patient;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the ventilation information, where the controller selects between a number of discrete lowpass cutoff frequencies, each lowpass cutoff frequency corresponding to a particular range of values of the heart rate.

37. The device of claim **36**, wherein the controller selects the cutoff frequency of the adaptive lowpass filter at approximately 0.5 Hz, 0.75 Hz, and 1.0 Hz when the heart rate is respectively approximately less than 29 beats per minute, between 68 and 88 beats per minute, and greater than 88 beats per minute.

38. The device of claim **36**, in which the signal processor includes:

an analog signal processing circuit, receiving the transthoracic impedance signal and including an analog-to-digital (A/D) converter providing a responsive digital transthoracic impedance signal; and

wherein the adaptive lowpass filter includes a digital 4-pole Chebyshev filter including a state-space structure.

39. The device of claim **36**, wherein the controller selects the cutoff frequency of the adaptive lowpass filter to be higher when the heart activity signal indicates a higher heart rate and lower when the heart activity signal indicates a lower heart rate.

40. A cardiac rhythm management system, including the cardiac rhythm management device of claim **36**, the cardiac rhythm management system further comprising:

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

41. The cardiac rhythm management system of claim **40**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

42. The cardiac rhythm management system of claim **41**, wherein the indifferent electrode is carried by a header portion of the housing.

43. A cardiac rhythm management device comprising:

an exciter, adapted to be coupled to a thorax of a patient for delivering stimuli thereto;

a signal processor, including a receiver for obtaining a transthoracic impedance responsive to the stimuli, the signal processor extracting ventilation information from the transthoracic impedance, wherein the signal processor includes an adaptive lowpass filter for removing a cardiac stroke component of the transthoracic impedance signal, a cutoff frequency of the adaptive lowpass filter being adaptively based on a heart rate of the patient, the cutoff frequency of the adaptive lowpass filter being independent of a breathing rate signal from the patient;

a therapy circuit, adapted to be coupled to a heart of the patient for delivering cardiac rhythm management therapy thereto; and

a controller, coupled to the therapy circuit for adjusting a rate of delivery of the cardiac rhythm management therapy based on the ventilation information;

an endocardial lead, carrying first and second electrodes, the lead being coupled to the cardiac rhythm management device; and

a housing, carrying the cardiac rhythm management device, the housing including third and fourth electrodes.

44. The cardiac rhythm management system of claim **43**, wherein the first electrode is a tip electrode, the second electrode is a ring electrode, the third electrode is a case electrode, and the fourth electrode is an indifferent electrode.

45. The cardiac rhythm management system of claim **44**, wherein the indifferent electrode is carried by a header portion of the housing.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO.: 6,161,042

DATED: Dec. 12, 2000

INVENTOR(S) : Hartley et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In column 4, lines 24-25, delete the paragraph break after "patient.".

In column 13, line 13, delete "AID" and insert --A/D--, therefor.

In column 18, line 46, delete "to bc" and insert --to be--, therefor.

In column 19, line 52, delete "AID" and insert --A/D--, therefor.

In column 22, line 59, delete "29 beats" and insert --68 beats--, therefor.

Signed and Sealed this

Twenty-ninth Day of May, 2001

Attest:

Nicholas P. Godici

Attesting Officer

NICHOLAS P. GODICI

Acting Director of the United States Patent and Trademark Office

APPENDIX #3

US Patent No. 6,574,507

US006574507B1

(12) **United States Patent**
Bonnet

(10) **Patent No.: US 6,574,507 B1**
(45) **Date of Patent: Jun. 3, 2003**

(54) **ACTIVE IMPLANTABLE MEDICAL DEVICE FOR TREATING SLEEP APNEA SYNDROME BY ELECTROSTIMULATION**

(75) Inventor: **Jean-Luc Bonnet**, Monrouge (FR)

(73) Assignee: **Ela Medical S.A.**, Montrouge (FR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/508,068**

(22) PCT Filed: **Jul. 5, 1999**

(86) PCT No.: **PCT/IB99/01345**

§ 371 (c)(1),
(2), (4) Date: **Mar. 6, 2000**

(87) PCT Pub. No.: **WO00/01438**

PCT Pub. Date: **Jan. 13, 2000**

(30) **Foreign Application Priority Data**

Jul. 6, 1998 (FR) 98 08639

(51) **Int. Cl.**[7] **A61N 1/365**

(52) **U.S. Cl.** **607/20**; 607/42

(58) **Field of Search** 600/508, 509, 600/529, 547; 607/9, 11, 16, 17, 20, 119, 42

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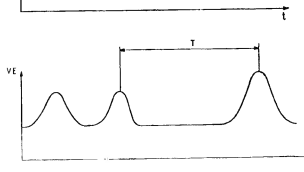
* cited by examiner

Primary Examiner—Mark Bockelman
(74) *Attorney, Agent, or Firm*—Orrick, Herrington & Sutcliffe LLP

(57) **ABSTRACT**

An active implantable medical device for electrostimulation in response to a determined sleep apnea syndrome, particularly a pacemaker. This device measures the respiratory activity of the patient, using for example, a minute ventilation sensor and/or a blood oxygen saturation sensor, and analyzes the sensor signal, to determine occurrence of an apnea according to the signal delivered by the sensor. The device also delivers an increase cardiiac pacing rate in the event of detection of apnea. The device also can deliver a neurological and/or cardiac stimulation so as to apply selectively to the patient an electric stimulus. The device also determines the patients's state of activity, according to predetermined criteria, such that the increased pacing rate is provided only during a sleep phase and otherwise inhibited. The analysis can in particular detect and occurrence of successive apnea during a phase of sleep and determine the occurrence of a sleep apnea syndrome when the number of apnea events detected during a given period of time exceeds a predetermined threshold.

31 Claims, 9 Drawing Sheets



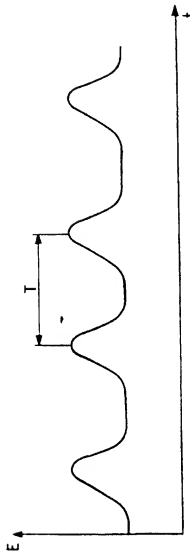


FIG_1

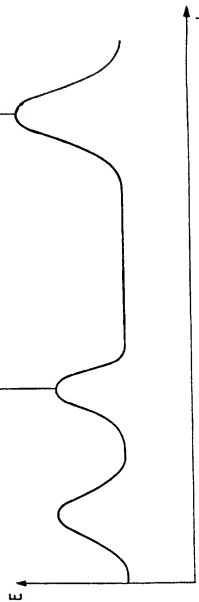


FIG_2

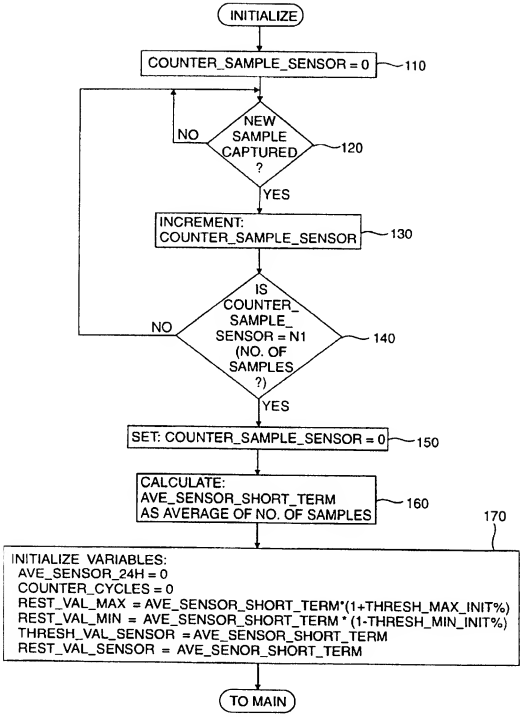
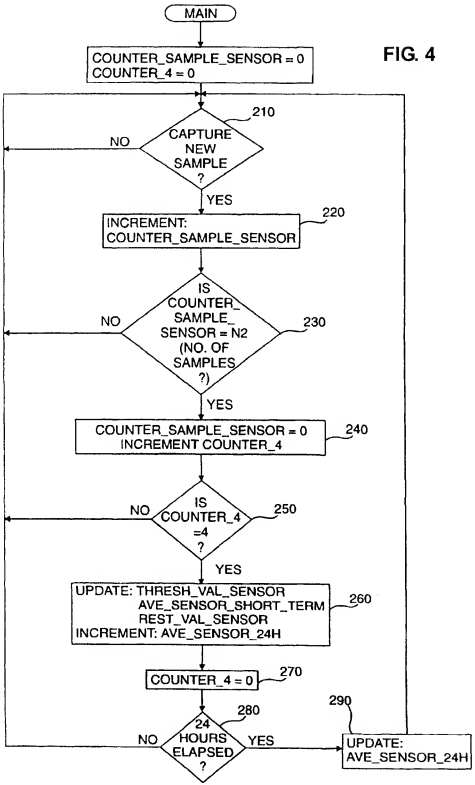

INITIALIZE
COUNTER_SAMPLE_SENSOR = 0
110
NEW SAMPLE CAPTURED ?
NO
120
YES
INCREMENT: COUNTER_SAMPLE_SENSOR
130
IS COUNTER_ SAMPLE_ SENSOR = N1 (NO. OF SAMPLES ?)
NO
140
YES
SET: COUNTER_SAMPLE_SENSOR = 0
150
CALCULATE: AVE_SENSOR_SHORT_TERM AS AVERAGE OF NO. OF SAMPLES
160
170
INITIALIZE VARIABLES:
AVE_SENSOR_24H = 0
COUNTER_CYCLES = 0
REST_VAL_MAX = AVE_SENSOR_SHORT_TERM*(1+THRESH_MAX_INIT%)
REST_VAL_MIN = AVE_SENSOR_SHORT_TERM * (1-THRESH_MIN_INIT%)
THRESH_VAL_SENSOR = AVE_SENSOR_SHORT_TERM
REST_VAL_SENSOR = AVE_SENOR_SHORT_TERM
TO MAIN

FIG. 3

FIG. 4


MAIN
COUNTER_SAMPLE_SENSOR = 0
COUNTER_4 = 0
210
CAPTURE NEW SAMPLE ?
NO
YES
220
INCREMENT: COUNTER_SAMPLE_SENSOR
IS COUNTER_SAMPLE_SENSOR = N2 (NO. OF SAMPLES ?)
230
NO
YES
COUNTER_SAMPLE_SENSOR = 0
INCREMENT COUNTER_4
240
IS COUNTER_4 =4 ?
250
NO
YES
UPDATE: THRESH_VAL_SENSOR
AVE_SENSOR_SHORT_TERM
REST_VAL_SENSOR
INCREMENT: AVE_SENSOR_24H
260
COUNTER_4 = 0
270
24 HOURS ELAPSED ?
280
NO
YES
290
UPDATE: AVE_SENSOR_24H

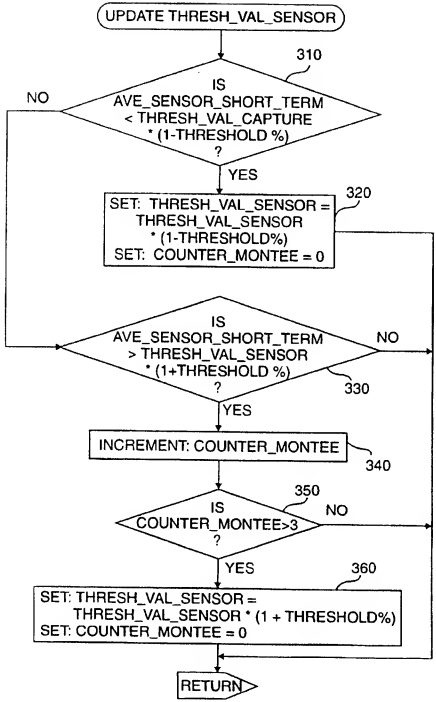

UPDATE THRESH_VAL_SENSOR
310
IS AVE_SENSOR_SHORT_TERM < THRESH_VAL_CAPTURE * (1-THRESHOLD %) ?
NO
YES
320
SET: THRESH_VAL_SENSOR = THRESH_VAL_SENSOR * (1-THRESHOLD%)
SET: COUNTER_MONTEE = 0
IS AVE_SENSOR_SHORT_TERM > THRESH_VAL_SENSOR * (1+THRESHOLD %) ?
NO
330
YES
INCREMENT: COUNTER_MONTEE
340
350
IS COUNTER_MONTEE>3 ?
NO
YES
360
SET: THRESH_VAL_SENSOR = THRESH_VAL_SENSOR * (1 + THRESHOLD%)
SET: COUNTER_MONTEE = 0
RETURN

FIG. 5

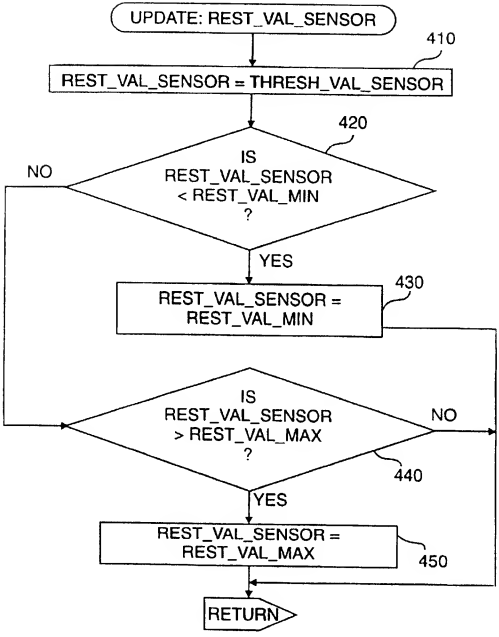

UPDATE: REST_VAL_SENSOR
410
REST_VAL_SENSOR = THRESH_VAL_SENSOR
420
IS REST_VAL_SENSOR < REST_VAL_MIN ?
NO
YES
430
REST_VAL_SENSOR = REST_VAL_MIN
IS REST_VAL_SENSOR > REST_VAL_MAX ?
NO
440
YES
REST_VAL_SENSOR = REST_VAL_MAX
450
RETURN

FIG. 6

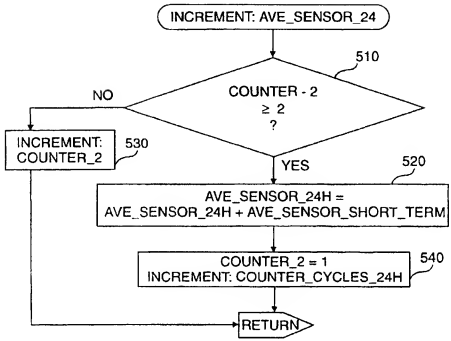

INCREMENT: AVE_SENSOR_24
510
COUNTER - 2
≥ 2
?
NO
YES
INCREMENT:
COUNTER_2
530
520
AVE_SENSOR_24H =
AVE_SENSOR_24H + AVE_SENSOR_SHORT_TERM
COUNTER_2 = 1
INCREMENT: COUNTER_CYCLES_24H
540
RETURN

FIG. 7

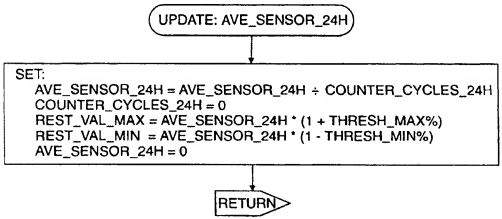

UPDATE: AVE_SENSOR_24H
SET:
AVE_SENSOR_24H = AVE_SENSOR_24H ÷ COUNTER_CYCLES_24H
COUNTER_CYCLES_24H = 0
REST_VAL_MAX = AVE_SENSOR_24H * (1 + THRESH_MAX%)
REST_VAL_MIN = AVE_SENSOR_24H * (1 - THRESH_MIN%)
AVE_SENSOR_24H = 0
RETURN

FIG. 8

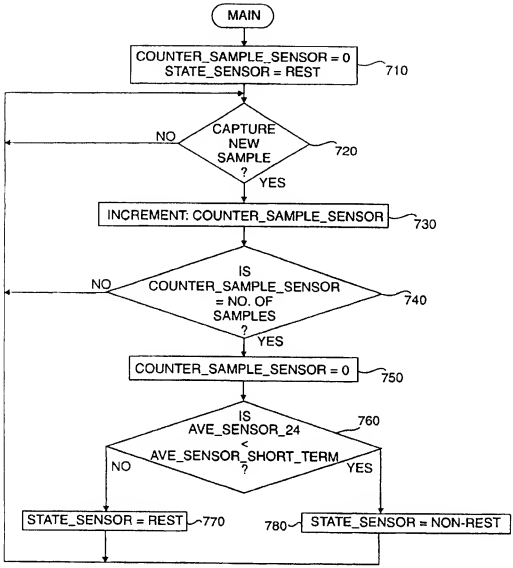

MAIN
COUNTER_SAMPLE_SENSOR = 0
STATE_SENSOR = REST
710
CAPTURE NEW SAMPLE ?
NO
YES
720
INCREMENT: COUNTER_SAMPLE_SENSOR
730
IS COUNTER_SAMPLE_SENSOR = NO. OF SAMPLES ?
NO
YES
740
COUNTER_SAMPLE_SENSOR = 0
750
IS AVE_SENSOR_24 < AVE_SENSOR_SHORT_TERM ?
760
NO
YES
STATE_SENSOR = REST
770
780
STATE_SENSOR = NON-REST

FIG. 9

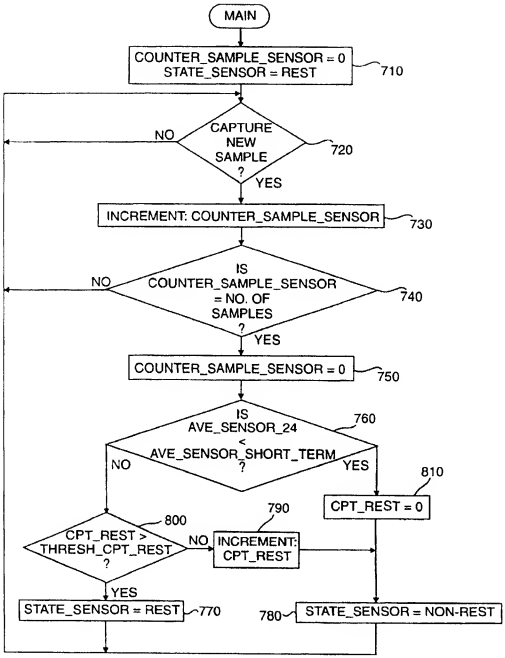

MAIN
COUNTER_SAMPLE_SENSOR = 0
STATE_SENSOR = REST
710
CAPTURE NEW SAMPLE ?
NO
YES
720
INCREMENT: COUNTER_SAMPLE_SENSOR
730
IS COUNTER_SAMPLE_SENSOR = NO. OF SAMPLES ?
NO
YES
740
COUNTER_SAMPLE_SENSOR = 0
750
IS AVE_SENSOR_24 < AVE_SENSOR_SHORT_TERM ?
760
NO
YES
CPT_REST = 0
810
CPT_REST > THRESH_CPT_REST ?
800
NO
INCREMENT: CPT_REST
790
YES
STATE_SENSOR = REST
770
780
STATE_SENSOR = NON-REST

FIG. 10

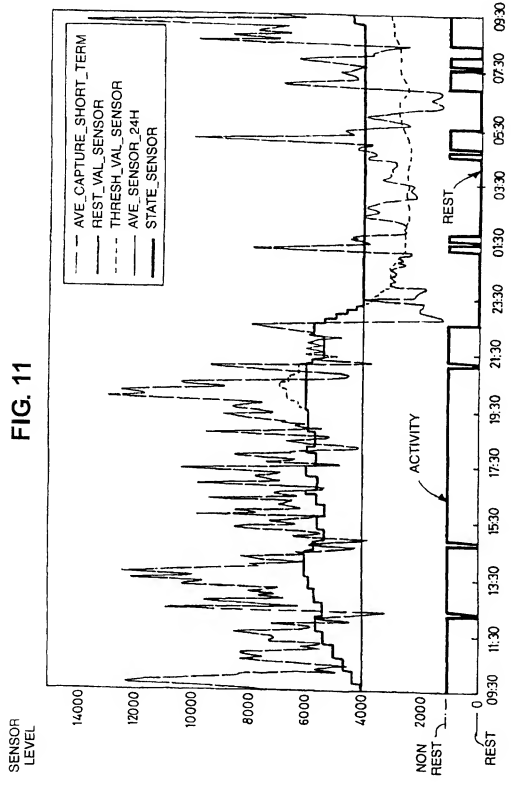

AVE_CAPTURE_SHORT_TERM
REST_VAL_SENSOR
THRESH_VAL_SENSOR
AVE_SENSOR_24H
STATE_SENSOR
SENSOR LEVEL
14000
12000
10000
8000
6000
4000
2000
0
NON REST
REST
09:30
11:30
13:30
15:30
17:30
19:30
21:30
23:30
01:30
03:30
05:30
07:30
09:30
ACTIVITY
REST

FIG. 11

ACTIVE IMPLANTABLE MEDICAL DEVICE FOR TREATING SLEEP APNEA SYNDROME BY ELECTROSTIMULATION

FIELD OF THE INVENTION

The present invention relates to the diagnosis of the syndrome of sleep apnea and more particularly, cardiac pacemakers able to detect sleep apnea and respond to the detection with electrostimulation.

BACKGROUND OF THE INVENTION

The syndrome of sleep apnea ("SAS"), more precisely the syndrome of obstructive and non central sleep apnea ("SOAS") is an affliction having generally as its origin an obstruction of the respiratory tracts. It is likely to involve a certain number of disorders such as painful and/or insufficient breathing, an abnormal heartbeat, and hypertension. Various treatments of SAS have been proposed, including treatments involving surgery, medication, and maintenance of a positive pressure in the respiratory tract by means of a facial mask worn during sleep.

One technique, as discussed in EP-A-0 702 979 (to Medtronic) proposes to treat SAS by electrostimulation. This document describes an implanted pulse generator, controlled by a sensor, which may be a dynamic pressure sensor or a sensor of intrathoracic impedance, making it possible to follow (monitor) the patient's respiration rate and thus to detect the occurrence of an apnea. When an apnea is detected, the generator delivers a salvo (sequence) of pulses to a stimulation electrode implanted in the muscles controlling the patient's airway. This technique is not, however, in practice, completely satisfactory. This is because the stimulation which is systematically started in the event of an increase in the intratracheal pressure, whatever the cause of this increase in pressure, and whether it is due to an SAS or not, will include inappropriate stimulations.

Pacemakers having a cardiac stimulation or pacing rate which is responsive to a detected physiological or physical parameter of the patient are known. Generally, as the measured parameter increases, it reflects an increasing level of activity of the patient (e.g., exercise), and the stimulation frequency increases so that the pacing rate is controlled to simulate the action of a normal heart. Once such style of pacing device measures the patient's so-called minute ventilation (minute volume) based on a transthoracic or intrathoracic impedance measurement. An earlier style of such a pacing device measured the respiration rate, but this parameter is generally believed to be less useful as a physiological parameter because it does not represent the patient's metabolic demand (also referred to as the cardiac output requirements) during phases of increased patient activity.

In the case of cardiac pacemakers, all these systems operate to increase the frequency of stimulation pulses when one detects an increasing activity of the patient wearing the device (i.e., the patient in which the device is implanted or on which the device is carried), and to decrease this frequency to a base value in the case of a diminution of activity, particularly during phases of rest of the patient.

EP-A-0 493 222 describes a process of correlation between, on the one hand, the two extreme values FC_{base} and X_{rest}, of the range of the stimulation frequency and, on the other hand, value X_{base} and X_{max}, which are respectively the rest value and the value of maximal activity, calculated from information collected by the sensor measuring the

detected physiological or physical parameter (also called an "enslavement sensor.") This process of correlation is known under the name of "automatic calibration of the enslavement", and the document describes a process to determine the value of X_{base} in the case of the utilization of the minute-ventilation as the parameter of enslavement. The value of the minute-ventilation at rest is then called MV_{rest}. This last value is obtained by the calculation of an average value during an interval on the order of 24 hours, including, therefore, periods of activity as well as periods of sleep of the wearer of the device.

It has been observed and recognized that, during phases of sleep, the values of MV_{rest} can be more than 50% below the values of this same parameter recorded during periods when the patient is awake (i.e., conscious) and active.

Many parameters, including, but not limited to, the minute ventilation, the respiratory frequency, the saturation of oxygen in the blood, the temperature, or the acceleration have been acceptably used as parameters of enslavement for control functions. In particular, these parameters have been used in the case of cardiac pacemakers, to vary the instantaneous frequency of the cardiac stimulation according to the measured or calculated parameter.

The utilization of one or more, and more particularly several, sensors, is at the expense of an incremental energy consumption. This is due to the additional hardware circuits, the increase of which is directly associated to the enslavement parameter transducer(s) (power supply, injection of current (as in the case of minute ventilation and other sensors), production and analysis of the signal, etc.), as well as the software used to process the sensor produced signals. It is generally realized that the microprocessors or specific circuits executing the software or logic functions are typically large, energy-consuming components when they execute algorithms to process data and make decisions.

As used herein, the terms "enslavement" and "enslaved" mean the control function has a determined result or output that varies as a function of the monitored parameter. The functional relationship may be linear, non-linear, defined by an algorithm or a look-up table, and may be predetermined or self-adjusting.

In the case of cardiac pacemakers, all these enslavement systems compete to increase the stimulation pulse frequency when one detects an increasing activity of the patient, and to decrease the stimulation pulse frequency to a base or minimum frequency in case of a diminution of activity, and particularly during phases of rest of the patient.

OBJECTS AND SUMMARY OF THE INVENTION

It is, therefore, an object of the invention to propose a device for the treatment of SAS by electrostimulation.

Broadly speaking, the present invention concerns analyzing the metabolic and functional state of the patient, for applying, selectively, a stimulation for the treatment of SAS only during the phases of patient activity where an SAS is really likely to appear, and otherwise inhibiting any SAS stimulation.

One aspect of the invention is directed to a device which is an active implantable medical pacemaker device allowing for the treatment by increased cardiac electrostimulation of the sleep apnea syndrome in a patient i.e., including: means for measuring the respiratory activity of the patient; means for analyzing and determining an occurrence of an apnea in response to the measured respiratory signal; and means for delivering an SAS stimulation, controlled by the analyzing

means, so as to apply selectively to the patient an increased cardiac stimulation rate in the event of a detection of an apnea. The SAS stimulation means is preferably a circuit which delivers SAS stimulation by increasing cardiac stimulation rate, and the respiratory activity measurement means may be a circuit which includes a minute ventilation sensor or a sensor which detects the oxygen saturation of the blood.

According to a preferred embodiment of the present invention, this device also includes means for determining a cardiac rate of the patient, including a rate in the absence of a determined apnea, means for determining a state of activity of the patient, this state being likely to take, according to predetermined criteria, a value representative of a state of sleep (also referred to as a rest phase) of the patient, such that the SAS stimulation means is triggerable only during a determined phase of sleep and otherwise is inhibited.

According to other various advantageous characteristics of the invention, the analyzing means detects an occurrence of a syndrome of sleep apnea when the number of apnea occurrences detected during a given period of time exceeds a predetermined threshold. In another embodiment, the determining means optionally determines a state of activity by analyzing the signal delivered by the means for measuring the respiratory activity of the patient, and/or by a separate auxiliary measurement means.

BRIEF DESCRIPTION OF THE DRAWINGS

Other features, characteristics and advantages of the present invention will appear to a person of ordinary skill in the art in view of the following description, which is made with reference to the drawings annexed, in which:

FIGS. **1** and **2** illustrate a signal representative of the respiration rate of the patient, in the absence of disorder and at the time of occurrence of an apnea respectively;

FIG. **3** is a flow chart of the initiallization phase of a process in accordance with an embodiment of the invention, which may be in response to an initial operation (start-up) or a manual re-initialization as may be initiated by a therapist;

FIG. **4** is a flow chart of a normal functioning phase, during the course of which one continuously determines different variables according to the invention;

FIG **5** is a flow chart of a process to update the variable THRESH1 VAL. SENSOR of the process illustrated in FIG. **3**;

FIG **6** is a flow chart of a process to update the variable REST_VAL._SENSOR of the process illustrated in FIG. **3**;

FIG **7** is a flow chart of a process to increment the variable AVE SENSOR_24H of the process illustrated in FIG. **3**;

FIG. **8** is a flow chart of a process to update the variable AVE SENSOR 24H of the process illustrated in FIG. **3**;

FIG **9** is a flow chart of a process to determine the variable STATE_SENSOR in the case of the utilization of a physiological parameter (ventilation—minute, temperature, etc.);

FIG. **10** is a flow chart of a process to determine the variable STATE_SENSOR in the case of the utilization of a non-physiological parameter such as acceleration; and

FIG **11** is an illustration showing the evolution over time of the different variables of the process of the invention, recorded during an exemplary 24 hour time interval.

DETAILED DESCRIPTION OF THE INVENTION

With reference to the drawing FIGS. **1** and **2**, an evolution of the respiration rate of a patient during sleep is shown. It is represented by the evolution over the course of time of the minute ventilation signal (signal VE, also called signal MV), which is a parameter obtained by a measurement of intrathoracic impedance that is predominantly physiological in nature. Although the minute ventilation signal is generally easy to implement for monitoring the respiration rate of the patient, other signals coming from other types of sensors can be used in the alternative or in addition to the minute ventilation sensor, for example, a sensor measuring blood oxygen saturation.

The measurement of the minute ventilation parameters is in itself well-known. The measurement is obtained between two electrodes placed in the rib cage, or if the implanted device is a pacemaker, between an electrode (for example, a stimulation electrode) and the case of the implanted medical device. The impedance is then measured in response to an injection of a constant current of a few hundreds of microamperes, at a frequency of a few hertz, typically 8 Hz. This technique is described, for example, by J. L. Bonnet et al., "Measurement of Minute-Ventilation with Different DDDR Pacemaker Electrode Configurations", PACE, Vol. 21, 98, Part 1, and it is implemented in the commercial rate responsive pacemaker devices sold under the trademark Chorus RM 7034, by ELA Médical, Montrouge, France.

One can determine, starting from this signal, a respiratory period T (FIG. **1**) which is defined as the time separating two detected impedance peaks. The peaks correspond to the high impedance obtained at the time of the inspiration (lungs being filled with air), and the decrease of the impedance corresponds to an expiratory phase.

Referring to FIG. **2**, a waveform representative of a minute ventilation signal recorded among patients suffering from sleep apnea is shown. These patients have normal expiratory phases, because the pulmonary pressure is sufficient to overcome the obstruction. On the other hand, the inspiration is abnormal because the lungs cannot fill with air.

One then can observe, as illustrated in FIG. **2**, an important lengthening of the respiratory period T after an expiration.

The first stage concerns diagnosing a sleep apnea occurrence. An apnea is classically defined as a respiratory pause of a duration that is greater than ten seconds, a phenomenon which is relatively easy to detect by monitoring minute ventilation. Moreover, this pause must occur during a sleep phase of the patient, because an apnea occurring while the patient is in an awake state cannot be caused by an SAS.

To respect the latter criterion, the invention proposes to discriminate between the sleep phase and the awake phase of the patient, and to apply an SAS therapy only during the sleep phase. Any treatment of an apnea which is detected during an awake phase is inhibited because, in this case, the apparent apnea normally is not pathological.

The sleep period can be diagnosed, of course, automatically, either starting from the signal delivered by the sensor monitoring the respiration activity of the patient, or by a separate sensor, for example, an activity sensor which measures a parameter which is predominantly physical such as acceleration as may be measured by an internal sensor located within the case.

EP-A-0 719 568 and its counterpart U.S. Pat. No. 5,622,428 commonly owned by ELA Medical describe in particular determining a "criterion of activity of a sensor", making it possible to make a distinction between the phases of rest (night or diurnal), and activity of the patient, in particular for contrast with a minute ventilation sensor. U.S. Pat. No. 5,622,428 is incorporated herein by reference in its entirety.

U.S. Pat. No. 5,622,428 discloses a process for distinguishing between different phases of rest of the wearer of the device, for example, rest during sleep periods and rest during awake periods, as well as other phases of activity, for example, activity during sleep and activity during awake periods and changing the operation of the device according to the detected phase.

With reference to FIG. **3**, the process of the phase of initialization is illustrated. The initialization phase process broadly concerns the calculation of several variables. It is noted that the calculation of certain variables (e.g., AVE_SENSOR_24H, THRESH_VAL_SENSOR and REST_VAL_SENSOR, that will be explained in more detail below), can be undertaken according to at least two different modes, depending on whether or not the device is in an initialization phase or in the regime of normal continuous functioning, which regime is referred to as "normal functioning phase".

The phase of initialization is brought out, i.e., used, when the medical device is first placed into operation, for example, at the time of implantation, or on a specific external command (i.e., a reset function, as may be delivered telemetrically in a known manner). The initialization phase has as its purpose and objective to endow the device with an initial value that will then be automatically and subsequently redetermined over time in the normal functioning phase.

In the initialization phase, the device acquires and stores in memory a predetermined number of minute ventilation values, corresponding, typically, to 32 samples of the measure of the minute—ventilation (steps **110** to **140**). Each sample corresponds to the determination of the minute—ventilation (MV) during a respiratory cycle. A counter referred to as COUNTER_SAMPLE_SENSOR is used to control the acquisition of the sample measures. The counter COUNTER_SAMPLE_SENSOR is reset to zero (step **100**) at the start of the initialization phase, and increments (step **130**) one count after each sample is successively acquired (step **120**).

When the value of the counter COUNTER_SAMPLE_SENSOR reaches the predetermined number N1, e.g., N1=32; the counter is reset to zero (step **150**) and the device then calculates an average of the 32 successively acquired values. This average is referred to as AVE_SENSOR_SHORT_TERM (step **160**).

At step **170**, the different variables used in the process of invention are then initialized. The counter COUNTER_CYCLES_24H and the variable AVE_SENSOR_24H are reset to 0, the variables THRESH_VAL_SENSOR and REST_VAL_SENSOR are set to the value AVE_SENSOR_SHORT_TERM that was determined at step **160**. The variable REST_VAL_MAX is set to a value that is related to the determined AVE_SENSOR_SHORT_TERM by a first predetermined coefficient (1+THRESH_MAX_INIT %), typically increased by 50%, and the variable REST_VAL_MIN is set to a value that is related to the determined AVE_SENSOR_SHORT_TERM by a second predetermined coefficient (1−THRESH_MIN_INIT %), typically decreased by 50%.

These initialized variables then serve as the initial values in the normal functioning phase, which is now described with reference to FIGS. **4** to **10**.

The general progress of the normal functioning phase is illustrated in a general manner in FIG. **4**. The implantable device executes the following steps: At step **200**, the two counters COUNTER_SAMPLE_SENSOR and COUNTER_4 are reset to zero, and in steps **210** to **250** a selected number N2 of successive samples as obtained by the sensor are collected and stored in a memory.

After **128** samples have been collected, that is to say after four repetitions of the collection of 32 samples, namely when COUNTER_SAMPLE_SENSOR=N2=32 and COUNTER_4=4 at step **250**, the device then updates the variables at step **260**. The variable THRESH_VAL_SENSOR is updated, in accordance with the process illustrated in the flow chart of FIG. **5**. The variable AVE_SENSOR_SHORT_TERM is calculated as an average of the 128 previously measured samples (it being understood that the, numbers of 128; 32 samples and 4 cycles, are exemplary and not limiting, and each can be replaced by a different value, as appropriate for the memory of the device and its processing power). The REST_VAL_SENSOR is updated in accordance with the process illustrated in the flow chart of FIG. **6**; and the variable AVE_SENSOR_24H is updated in accordance with the process illustrated in the flow chart of FIG. **7**.

Referring to FIG. **5**, the periodic update of the variable THRESH_VAL_SENSOR in a preferred embodiment is described. First, this variable serves to determine the level of activity of the sensor at the end of step **260**, that is to say after 128 cycles of sample measurement. It is used in addition for the calculation of variables REST_VAL_SENSOR and AVE_SENSOR_24H. It is calculated of the following manner. If the value of AVE_SENSOR_SHORT_TERM is comprised within the limits bounded by THRESH_VAL_SENSOR±THRESHOLD % (where the THRESHOLD % is a predetermined value, typically 6.25%), then THRESH_VAL_SENSOR is not modified (steps **310** and **330**). If, however, the value of AVE_SENSOR_SHORT_TERM has become less than THRESH_VAL_SENSOR_THRESHOLD %, one considers that the acquired (sensed) activity level has decreased, and one decreases then the variable THRESH_VAL_SENSOR by a quantity THRESHOLD %, and resets to zero the counter COUNTER_MONTEE (steps **310** and **320**), and if the value of AVE_SENSOR_SHORT_TEPM has become greater than THRESH_VAL_SENSOR+THRESHOLD %, then one increases the counter COUNTER_MONTEE by one count (steps **310**, **330** and **340**).

If the counter COUNTER_MONTEE reaches a predetermined count value, e.g., 4 (a number chosen in an arbitrary manner, but corresponding to a typical situation), one considers that the sensed activity level has increased, and one increases then THRESH_VAL_SENSOR by a quantity THRESHOLD %, and resets to zero COUNTER MONTEE (steps **350** and **360**).

Referring to FIG. **6**, the periodic update of the variable REST_VAL_SENSOR is described. The value REST_VAL_SENSOR has a default value which is the previously determined THRESH_VAL_SENSOR at step **410**.

But REST_VAL_SENSOR is nevertheless limited to two limits depending on then the value of REST_VAL_SENSOR is set equal to the value of REST_VAL_MIN (steps **420** and **430**), If REST_VAL_SENSOR is greater than REST_VAL_MAX, then the value of REST_VAL_SENSOR is set equal to the value REST_VAL_MAX (steps **420**, **440** and **450**). The determination of the values REST_VAL_MIN and REST_VAL_MAX are explained hereafter, with reference to FIG. **8**, especially in the ease where these values do not correspond to those established during the initialization phase (step **170**).

Referring to FIGS. **7** and **8**, the determination of the variable AVE_SENSOR_24H is described. This variable is

first incremented in manner specified on the flow chart of FIG. **7**, which is implemented during the course of step **260** of the process shown in FIG. **4**. Following the value of COUNTER_2 (a counter that can have only two values, e.g., 1 or 2), one increases the variable AVE_SENSOR_24H by the value of AVE_SENSOR_SHORT_TERM at step **520**, and one increments a counter COUNTER_CYCLES_24H at step **540**.

At the end of a period of 24 hours (**step 280** of FIG. **4**), which is calculated from either an internal clock signal of the device or from a number of iterations of preceding phases corresponding approximately to a duration of 24 hours, the device updates the variable AVE_SENSOR_24H (**step 290** of FIG. **4**).

The different operations resulting in this update of AVE_SENSOR_24H are clarified in step **610** of FIG. **8**. More precisely, the variable AVE_SENSOR_24H takes the value of the average of the sum of AVE_SENSOR_24H established at step **520**, an average that is calculated by dividing the total of the sum by the value COUNTER_CYCLES_24H determined at step **540**, as described above (FIG. **7**).

At step. **610** (FIG. **8**), the device then sets the values REST_VAL_MAX and REST_VAL_MIN, calculated from preceding result by the value AVE_SENSOR_24H. The maximal value, REST_VAL_MAX, of the REST_VALUE range, is set equal to AVE_SENSOR_24Hx(1+THRESH_MAX %), typically THRESH_MAX is a predetermined value, e.g. 50%. The minimal value, REST_VAL_MIN, of the REST_VALUE range is set equal to AVE_SENSOR_24Hx(1−THRESH_MIN %). Typically THRESH_MIN % is a predetermined value and may be, e.g., 0.

At the end of the step **610**, AVE_SENSOR_24H and COUNTER_CYCLES_24H are initialized to zero.

One will note that the determination of the variable REST_VALUE, in combination with the two extreme variation boundary limits REST_VAL_MAX and REST_VAL_MIN (themselves dependent on the variable AVE_SENSOR_24H) allows to establish, in a manner perfectly appropriate, the low point of the automatic calibration curve of the enslavement function that is described in the aforementioned EP-A-0 493 222, which is incorporated herein by reference, where one will be able to make correspond to define a relationship between REST_VALUE and the frequency of stimulation Fe_{base} programmed by the therapist.

The "criterion of sensor activity" defined above, corresponding in a variable STATE_SENSOR, is determined in accordance with the flow chart illustrated in FIGS. **9** or **10**, depending on the type of enslavement sensor used.

After a phase of initialization (**step 710**) and after a number of cycles corresponding to the value of COUNTER_SAMPLE_SENSOR, that is, typically after 32 cycles (steps **720** to **750**), the device compares the variable AVE_SENSOR_24H and AVE_SENSOR_SHORT_TERM (step **760**). If AVE_SENSOR_SHORT_TERM is less than AVE_SENSOR_24H, the device considers that the average level of activity for that period is below the average level of activity over a period 24 hours, and, therefore, the patient is reliably determined to be in a proven rest state (for example, a nocturnal sleep phase). The device then sets the value of STATE_SENSOR to "Rest" (step **770**). In the opposite case, it considers that there is no rest, that the patient is alert and active, and sets the value of STATE_SENSOR to "Non-Rest" (**step 780**).

For a non-physiological sensor (for example, a sensor of acceleration), the flow chart of FIG. **9** is slightly modified, as in the manner illustrated in FIG. **10**. In this case, a counter CPT_REST is employed; it is reset to zero at the initial step **710** and incremented (step **790**) each time that the device determines that the patient is in a proven state of rest. If this situation repeats a predetermined number of times, designated THRESH_CPT$_{13}$ REST, typically on the order 12 repetitions during the 24 hour period (**step 800**), then the value of STATE_SENSOR is set to "Rest" (step **770**). In the opposite case, one re-initializes CPT_REST to 0 (**step 810**) and sets STATE_SENSOR to "Non-Rest" (**step 780**). One will note incidentally that the flow chart of FIG. **9**[7] corresponds in fact to a simplified version of that of FIG. **10**, with THRESH_CPT_REST=0.

In an alternative embodiment, one can replace the counter incrementation and the test of the number of occurrences of samples acquired, by a test conducted over a fixed period defined by the internal clock of the device, for example, a fixed period of 10 minutes can be used to acquire the data used to calculate the short term average.

FIG. **11** illustrates an example of the evolution of the different variables THRESH_VAL_SENSOR, AVE_SENSOR_SHORT_TERM, REST_VAL_SENSOR and AVE_SENSOR_24H, over a 24 hour period as well as of the activity criterion STATE_SENSOR determined accordingly to the process of the invention. One can note that, during the phase of sleep between 23:00 hours (11:00 pm) and 6:00 hours (6:00 am), the variable STATE_SENSOR is preponderantly set to the state "Rest", and includes Non-Rest states.

The information given by the variable STATE_SENSOR thus will be able to be used by the device to trigger various functions necessitating or exploiting the knowledge of the Rest phases of the wearer of the device. It will be appreciated that by the use of additional thresholds, averages, and coefficients, multiple states of relative rest and activity may be defined for use by the device.

The EP-A-0 750 920 and its counterpart U.S. Pat. No. 5,722,996 and EPA-0 770 407 and its counterpart U.S. Pat. No. 5,766,228 both commonly assigned to ELA Medical, describe medical devices using combined information of a physiological sensor and a physical sensor, in particular a minute ventilation sensor and an accelerometer, to determine a state of a activity or a state of rest of the patient. U.S. Pat. Nos. 5,722,996 and 5,766,228 are incorporated herein by reference in their entirety.

Thus, having diagnosed an apnea, and having confirmed that this apnea is a sleep apnea, one then can carry out a calculation of an index of apnea. In this regard, when the apnea index exceeds a predetermined threshold, for example, more than ten apnea occurrences per hour (this threshold number can, of course, be programmable to be suitable for the particular patient), the presence of an SAS is determined. As soon as an SAS is diagnosed, an electric stimulation is then applied to the patient to compensate for the harmful effects of the SAS.

The electric stimulation can be a muscular stimulation (as described, for example, in the EP-A-0 702979 mentioned above or a neurological stimulation, to cause the immediate opening of the esophagus in order to allow inspiration. In the latter case, a neurological stimulation preferably will be applied only during the inspiratory phases of the patient's breathing cycle so as not to disturb the expiratory phase.

One also can envisage an embodiment whereby a stimulation is delivered only if the inspiratory period exceeds a preset value, for example, six seconds.

Further, in the preferred embodiment, the electric stimulation is a cardiac stimulation, for example, to accelerate the

heart rate (frequency) of the myocardium, to compensate for the effects of the SAS. Such a cardiac stimulation will be applied to as soon as an SAS is diagnosed, by increasing the stimulation frequency by a few beats per minute (typically+10 bpm), compared to the natural sinusal rate of the patient. The number of beats is preferably at least 10 beats higher. Such a device includes means for determining. a cardiac rate of the patient. The stimulation at the higher rate is applied for a given period of time, for example, sixty seconds and afterwards the device reverts to the former mode of operation, e.g., the lower stimulation frequency. It also should be understood that the increased cardiac stimulation can be applied together with a muscular and/or a neurological stimulation in response to a determined SAS.

A first sensing circuit determines a state of activity of the patient. This determination may be made, for example, by comparing the first sensor output signals to predetermined criteria which is a calculated value representative of a patient state of activity, in which case the state of activity of the sensor is determined. Alternatively, the first sensor circuit may compare the parameter calculated from the first sensor output signals to a predetermined criteria which is a calculated value representative of a patient state of activity in which case the activity level of the patient is determined. In each case, the predetermined criteria is representative of a state of rest of the patient, such that it is used to discriminate a level of patient activity corresponding to rest from a level of activity corresponding to non-rest.

The sensing circuit comprises substantially all of logic and hardware elements required to operate the sensor to sense the parameter and produce output signals corresponding to the sensed parameter, and to deliver a signal utilizable by the main circuit of the pacemaker. The main circuit includes a microprocessor and memory (RAM and/or ROM), as well as conventional latches, registers and power supplies (not shown) for processing the information for the enslavement of the stimulation frequency.

Furthermore, the preferred embodiment of the process described herein is implemented in an architecture including a microprocessor having associated software instructions stored in memory (ROM) and analog and digital logic circuits that are themselves known. Such an architecture is, for example, employed in dual chamber cardiac pacemakers sold under the trade name CHORUS, manufactured by ELA Medical.

Although it does not present all of the advantages of the preferred solution with a microprocessor, a design in hard-wired discrete circuits having dedicated logic circuits is nevertheless perfectly foreseeable, and equally within the framework of the present invention.

One skilled in the art should understand that the invention is not limited to the disclosed embodiments, which are presented for purposes of illustration and not of limitation.

I claim

1. A cardiac stimulation device for treating the syndrome of the sleep apnea of a patient by electrostimulation comprising:

means for measuring the respiratory activity of the patient having an output signal representative of the patient's respiratory activity;

means for analyzing the patient's respiratory activity according to the output signal from the respiratory measuring means to determine an occurrence of an apnea;

means for determining a cardiac rate of the patient, including a second rate in the absence of a determined apnea;

means for stimulation, controlled by the analyzing means, to apply selectively to the patient cardiac stimuli at a first rate in the event of a detection of an apnea, said first rate being higher than the second rate;

means for determining a state of activity of the patient, said state being selected, according to predetermined criteria, from among a first value representative of a sleep state of the patient and a second value representative of an awake state of the patient;

wherein the stimulation means is applying to the patient cardiac stimuli at the first cardiac rate only during a determined sleep phase.

2. The device of claim **1** in which the stimulation means stimulates in response to being triggered at the first rate, wherein the first rate is at least 10 beats higher than the second rate.

3. The device of claim **1**, in which the analyzing means detects an occurrence of successive apnea during a sleep phase and determines an occurrence of a syndrome of apnea of the sleep when the number of apnea detected during a given period of time exceeds a predetermined threshold.

4. The device of claim **1**, in which the means of determination of a state of activity further comprises analyzing the output signal from said measuring means.

5. The device of claim **1**, further comprising an auxiliary measuring means for measuring a state of activity of the patient; wherein the means for determining the state of activity further comprises means for analyzing the output signal from the auxiliary measuring means, said auxiliary measuring means output signal being distinct from said means for measuring of the respiratory activity of the patient.

6. The device of claim **1**, further comprising an auxiliary means for measuring a state of activity of the patient, wherein said auxiliary measuring means further comprises an accelerometer.

7. The device of claim **1**, wherein the means for measuring the respiratory activity of the patient further comprises a minute ventilation sensor.

8. The device of claim **1**, wherein the means for measuring the respiratory activity of the patient further comprises a sensor of oxygen saturation of blood.

9. A cardiac stimulation device for treating a sleep apnea syndrome of a patient by electrostimulation comprising:

means for determining a state of activity of the patient, said state being selected, according to predetermined criteria, from among a first value representative of a sleep state of the patient and a second value representative of an awake state of the patient;

means for measuring the respiratory activity of the patient;

means for determining an occurrence of an apnea based upon said measured respiratory activity;

means for determining a cardiac rate of the patient during an identified sleep state as a second rate;

means for providing a first rate for cardiac stimulation as the second rate incremented by a first number of beats per minute; and

means for selectively applying cardiac stimulation at said first rate to the patient in response to a determined apnea during a sleep state.

10. The device of claim **9** wherein the first number of beats is at least 10 beats per minute.

11. The device of claim **10** wherein the first number of beats is 10 beats per minute.

12. The device of claim **9**, wherein the apnea determining means determines an occurrence of successive apnea during

a sleep phase and determines an occurrence of a syndrome of sleep apnea when the number of apnea detected during a given period of time exceeds a predetermined threshold.

13. The device of claim **9**, wherein the means for determining a state of activity further comprises means for analyzing the measured respiration activity.

14. The device of claim **9**, further comprising an auxiliary measuring means for measuring a state of activity of the patient having output signal; wherein the means for determining the state of activity further comprises means for analyzing the output signal from the auxiliary measuring means, said auxiliary measuring means output signal being distinct from said means for measuring of the respiratory activity of the patient.

15. The device of claim **14**, wherein said auxiliary means for measuring a state of activity further comprises an accelerometer.

16. The device of claim **9**, further comprising an auxiliary means for measuring a state of activity of the patient, wherein said auxiliary measuring means further comprises an accelerometer.

17. The device of claim **9**, wherein the means for measuring the respiratory activity of the patient further comprises a minute ventilation sensor.

18. The device of claim **9**, wherein the means for measuring the respiratory activity of the patient further comprises a sensor of oxygen saturation of blood.

19. The device of claim **9**, wherein the means for selectively applying cardiac stimulation at said first rate applies said first rate for a predetermined time.

20. The device of claim **9**, wherein the means for determining said second rate further comprises means for determining a natural sinusal rate of the patient.

21. A cardiac stimulation device for treating a sleep apnea syndrome of a patient by electrostimulation comprising:

a patient activity detector having predetermined criteria corresponding to a sleep state of a patient and an awake state of the patient, said detector monitoring patient activity and producing a first state output when the patient is in a sleep state and a second state output when the patient is in an awake state;

a respiratory activity monitor having a first activity output corresponding to a patient's respiratory activity;

an apnea detector responsive to said first activity output for determining an occurrence of an apnea based upon said patient respiratory activity;

a cardiac rate monitor for determining a first cardiac rate of the patient in response to the patient activity monitor producing the first state output;

a cardiac stimulator having a second cardiac stimulation rate output corresponding to the determined first cardiac rate incremented by a first number of beats per minute, said stimulator applying cardiac stimulation at said cardiac stimulation rate to the patient in response to a determined apnea and the patient activity monitor producing the first state output.

22. The device of claim **21** wherein the first number of beats is at least 10 beats per minute.

23. The device of claim **22** wherein the first number of beats is 10 beats per minute.

24. The device of claim **21**, wherein the apnea detector has a predetermined count and a given time period and determines an occurrence of a syndrome of sleep apnea occurrences when the number of apnea detected while the patient activity monitor produces the first state output during the given period of time exceeds the predetermined count.

25. The device of claim **21**, wherein the patient activity detector further comprises means for analyzing a respiratory activity monitor output.

26. The device of claim **21**, further comprising an auxiliary patient activity monitor distinct from said respiratory activity monitor having a second activity output corresponding to a state of activity of the patient; wherein the means for determining the state of activity further comprises means for analyzing the second activity output in determining the patient's activity state.

27. The device of claim **26**, wherein said auxiliary patient activity monitor further comprises an accelerometer.

28. The device of claim **21**, wherein the respiratory activity monitor further comprises an electrode pair, a current injector connected in the electrode pair, a voltage detector connected to the electrode pair, and a controller operating the current injector to inject a current pulse and the voltage detector to detect a voltage in response to the current, wherein the controller calculates a minute ventilation based on the detected voltages.

29. The device of claim **21**, wherein the respiratory activity monitor further comprises a sensor of oxygen saturation of blood.

30. The device of claim **21**, wherein the cardiac stimulator applies cardiac stimulation at said cardiac stimulation rate for a predetermined time.

31. The device of claim **21**, wherein the cardiac rate monitor determines a natural sinusal rate of the patient as said first cardiac rate.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,574,507 B1
DATED : June 3, 2003
INVENTOR(S) : Jean-Luc Bonnet

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 1,
Line 45, delete "Once" and insert -- one such -- therefor;

Column 3,
Line 4, after "increasing" insert -- the --;

Column 6,
Line 12, delete "the, numbers" and insert -- the numbers -- therefor;
Line 38, delete "SHORT-TEPM" and insert -- SHORT-TERM -- therefor;
Line 56, after "depending on" insert -- AVE_SENSOR_24H, such that: If REST_VAL_SENSOR is less than REST_VAL_MIN --;

Column 7,
Line 1, delete "in manner" and insert -- in the manner -- therefor;
Line 24, delete "from preceding" and insert -- from the preceding -- therefor;
Line 27, delete "THRESH MAX" and insert -- THRESH_MAX -- therefor;
Line 59, delete "period 24" and insert -- period of 24 -- therefor,

Column 8,
Line 6, delete "THRESH_CPT$_{13}$ REST" and insert -- THRESH_CPT_REST -- therefor;
Line 6, delete "order 12" and insert -- order of 12 -- therefor;
Lines 23-24, delete "accordingly" and insert -- according -- therefor;

Column 9,
Line 3, delete "applied to" and insert -- applied -- therefor;
Line 7, delete "determining. a" and insert -- determining a -- therefor.

Signed and Sealed this

Third Day of May, 2005

JON W. DUDAS
Director of the United States Patent and Trademark Office

RELATED PROCEEDINGS APPENDIX

None.